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# Needle Acupuncture for Substance Use Disorders

## A Systematic Review

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14. ABSTRACT

**This systematic review synthesized evidence from trials of needle acupuncture to provide estimates of the effectiveness of needle acupuncture for substance use disorders (PROSPERO record CRD42015016040). In November 2014, we searched PubMed, PsycINFO, CINAHL, AMED, CENTRAL MANTIS, and Embase, as well as bibliographies of existing systematic reviews and included studies, to identify English-language reports of randomized controlled trials (RCTs) testing the efficacy and safety of needle acupuncture???used adjunctively or as monotherapy???to treat adults diagnosed with alcohol, opioid, stimulant, and/or cannabis use disorder. Two independent reviewers screened identified literature using predetermined eligibility criteria, abstracted studylevel information, and assessed the methodological quality of included studies. Outcomes of interest included relapse, quantity and frequency of substance use, withdrawal symptoms treatment dropout, functional status and quality of life, and adverse events. When possible, metaanalyses and meta-regressions were conducted using the Hartung-Knapp-Sidik-Jonkman method for random-effects models. Quality of evidence was assessed using the GRADE approach.**

**Forty-one studies (reported in 48 publications) with 5,227 participants were included. When the data were pooled across studies, no significant effects of acupuncture (as adjunctive or monotherapy versus any comparator) versus any comparator were observed at postintervention for relapse (SMD ???0.12; 95% CI ???0.46 to 0.22; 10 RCTs), frequency of substance use (SMD ???0.27; CI ???2.67 to 2.13; 2 RCTs), quantity of substance use (SMD 0.01; CI ???0.40 to 0.43; 3 RCTs), or treatment dropout (OR 0.82; CI 0.63 to 1.09; 22 RCTs). We did identify statistically significant, clinically medium effects in favor of acupuncture (as an adjunctive or monotherapy) versus any comparator at postintervention for withdrawal/craving (SMD ???0.57, CI ???0.93 to ???0.20; 20 RCTs) and anxiety (SMD ???0.74, CI ???1.15 to ???0.33; 6 RCTs), though pooled effects were not statistically significant at longer follow-up points. Only 12 RCTs provided safety data these data suggest that acupuncture is not typically associated with serious adverse events though some participants may experience slight bleeding/pain at the needle insertion site. Metaregressions indicated that treatment dropout results differed by substance targeted, and withdrawal/craving symptoms and treatment dropout differed by acupuncture type. We found no evidence to suggest that effects of needle acupuncture differed systematically by acupuncture when offered as adjunctive versus monotherapy or by type of comparator (treatment as usual sham acupuncture, passive comparator, active comparator). All of the above results are limited however, by low or very low quality of evidence and the limited power to detect**

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# Preface

The Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury is interested in determining the efficacy and comparative effectiveness of integrative medicine approaches for psychological health conditions. This document is a systematic review of needle acupuncture for substance use disorders, conducted as part of a two-year project on integrative medicine approaches for psychological health conditions. The review will be of interest to military health policymakers and practitioners, civilian health care providers and policymakers, payers, and patients.

A version of this report was provided to the committee for review in March 2015; we reproduce that version here, with minor editorial updates. None of the authors has any conflict of interest to declare.

This research was sponsored by the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury and conducted within the Forces and Resources Policy Center of the RAND National Defense Research Institute, a federally funded research and development center sponsored by the Office of the Secretary of Defense, the Joint Staff, the Unified Combatant Commands, the Navy, the Marine Corps, the defense agencies, and the defense Intelligence Community. For more information on the RAND Forces and Resources Policy Center, see http://www.rand.org/nsrd/ndri/centers/frp.html or contact the director (contact information is provided on the web page).

# Abstract

This systematic review synthesized evidence from trials of needle acupuncture to provide estimates of the effectiveness of needle acupuncture for substance use disorders (PROSPERO record CRD42015016040).

In November 2014, we searched PubMed, PsycINFO, CINAHL, AMED, CENTRAL, MANTIS, and Embase, as well as bibliographies of existing systematic reviews and included studies, to identify English-language reports of randomized controlled trials (RCTs) testing the efficacy and safety of needle acupuncture—used adjunctively or as monotherapy—to treat adults diagnosed with alcohol, opioid, stimulant, and/or cannabis use disorder. Two independent reviewers screened identified literature using predetermined eligibility criteria, abstracted study-level information, and assessed the methodological quality of included studies. Outcomes of interest included relapse, quantity and frequency of substance use, withdrawal symptoms, treatment dropout, functional status and quality of life, and adverse events. When possible, meta-analyses and meta-regressions were conducted using the Hartung-Knapp-Sidik-Jonkman method for random-effects models. Quality of evidence was assessed using the GRADE approach.

Forty-one studies (reported in 48 publications) with 5,227 participants were included. When the data were pooled across studies, no significant effects of acupuncture (as adjunctive or monotherapy versus any comparator) versus any comparator were observed at postintervention for relapse (SMD −0.12; 95% CI −0.46 to 0.22; 10 RCTs), frequency of substance use (SMD −0.27; CI −2.67 to 2.13; 2 RCTs), quantity of substance use (SMD 0.01; CI −0.40 to 0.43; 3 RCTs), or treatment dropout (OR 0.82; CI 0.63 to 1.09; 22 RCTs). We did identify statistically significant, clinically medium effects in favor of acupuncture (as an adjunctive or monotherapy) versus any comparator at postintervention for withdrawal/craving (SMD −0.57, CI −0.93 to −0.20; 20 RCTs) and anxiety (SMD −0.74, CI −1.15 to −0.33; 6 RCTs), though pooled effects were not statistically significant at longer follow-up points. Only 12 RCTs provided safety data; these data suggest that acupuncture is not typically associated with serious adverse events, though some participants may experience slight bleeding/pain at the needle insertion site. Meta-regressions indicated that treatment dropout results differed by substance targeted, and withdrawal/craving symptoms and treatment dropout differed by acupuncture type. We found no evidence to suggest that effects of needle acupuncture differed systematically by acupuncture when offered as adjunctive versus monotherapy or by type of comparator (treatment as usual, sham acupuncture, passive comparator, active comparator). All of the above results are limited, however, by low or very low quality of evidence and the limited power to detect statistically significant differences due to the number of studies and amount of participants within studies.

The available evidence suggests no consistent effect of acupuncture versus comparator interventions on substance use outcomes. There were positive effects for withdrawal symptoms and anxiety, yet these results were based on low or very low quality of evidence.

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# Summary

## Introduction

Substance use disorders (SUDs) are prevalent among U.S. adults (Compton et al., 2007; Grant et al., 2004; Hasin et al., 2007; Kessler et al., 2005) and can have significant health, social, and economic consequences (National Institute on Drug Abuse, 2008). The use of acupuncture for treating SUDs has significantly increased in recent decades (Lu et al., 2009), with numerous randomized controlled trials (RCTs) assessing its efficacy. This systematic review synthesized evidence from trials of needle acupuncture to provide estimates of the effectiveness of needle acupuncture for treating SUDs (PROSPERO record CRD42015016040).

This review was specifically guided by the following key questions (KQs):

- *KQ 1*: What are the efficacy and safety of needle acupuncture, as an adjunctive or monotherapy, in reducing the frequency and quantity of substance use, withdrawal symptoms, treatment dropout, relapse, functional status, and quality of life in adults with alcohol, opioid, stimulant, or cannabis use disorders compared with active treatments, sham acupuncture, treatment as usual (TAU), wait lists, or no treatment?
  - *KQ 1a*: Does the effect of needle acupuncture vary by the substance targeted (i.e., alcohol, opioids, stimulants, or cannabis)?
  - *KQ 1b*: Is one type of needle acupuncture (e.g., auricular acupuncture) more effective than others?
  - *KQ 1c*: Is needle acupuncture more effective as an adjunctive therapy than as a monotherapy?
  - *KQ 1d*: Does the effect of needle acupuncture on SUDs depend on the comparator?

## Methods

To answer our key questions, we conducted a systematic search of electronic databases (PubMed, PsycINFO, CINAHL, AMED, CENTRAL, MANTIS, and Embase) from their inception to November 2014, as well as bibliographies of existing systematic reviews and included studies, to identify English-language reports of RCTs testing the efficacy and safety of needle acupuncture—used adjunctively or as monotherapy—to treat individuals with SUDs. Participants must have been 18 years or older and diagnosed with alcohol, opioid, stimulant, and/or cannabis use disorder. There were no exclusion criteria regarding comparison intervention or trial setting.

Two independent reviewers screened the identified literature using predetermined eligibility criteria, abstracted prespecified study-level information and outcome data, and assessed the quality of included studies. Outcomes of interest included quantity and frequency of substance use, withdrawal or craving symptoms, treatment dropout, relapse, functional status, health-

related quality of life, and adverse events. When possible, meta-analyses and meta-regressions were conducted using the Hartung-Knapp-Sidik-Jonkman method for random-effects models. Quality of evidence was assessed using the Grades of Recommendation, Assessment, Development, and Evaluation (or GRADE) approach.

## Results

We identified 41 eligible RCTs (reported in 48 publications), conducted in 12 countries with 5,227 participants. All studies took place SUD specialty care settings, with 20 studies taking place in outpatient settings and 21 in inpatient settings. Participants' average age ranged from approximately 28 to 45 years old. One RCT had only females, and ten RCTs had only males; of the remaining RCTs, the proportion of males ranged from 50.3 to 93.8 percent.

### *Key Question 1*

We identified 41 RCTs providing data on the overall efficacy of acupuncture and 12 RCTs providing data on the overall safety of acupuncture. No consistent significant effects were found for any acupuncture (as an adjunctive or monotherapy) versus any comparator for substance use relapse, frequency of substance use, and quantity of substance use at postintervention. We did identify statistically significant, clinically medium effects in favor of acupuncture (as an adjunctive or monotherapy) versus any comparator at postintervention for withdrawal/craving (standardized mean difference [SMD] −0.57; 95% confidence interval [CI] −0.93 to −0.20; 20 RCTs) and functional status (anxiety) (SMD −0.74; CI −1.15 to −0.33; 6 RCTs), though pooled effects were not statistically significant at longer follow-up points, and postintervention results were based on low or very low quality of evidence due to attrition bias, high heterogeneity, and/or wide confidence intervals. (Note: All CIs reported in this study are at the 95-percent level.) No significant effects were found for health-related quality of life or treatment dropout. The available evidence on adverse events is very limited; of those 12 RCTs reporting safety data, we did not find strong evidence indicating that acupuncture is associated with any serious adverse events, though a small proportion of participants experienced mild adverse events (e.g., slight bleeding/pain at acupuncture site).

### *Key Question 1a*

For KQ 1a on the effect of needle acupuncture by substance targeted, we identified 11 RCTs reporting on alcohol use specifically, ten RCTs on stimulant use specifically, 13 RCTs on opioid use specifically, and one RCT on cannabis use specifically. Indirect comparisons via meta-regressions of the results of analyses by substance targeted yielded no statistically significant differences in effects by substance targeted for relapse, withdrawal/craving, and functional status. There were some differences in the effect of acupuncture on treatment dropout by substance targeted; studies targeting alcohol use showed a greater benefit from acupuncture on

treatment dropout than studies focusing on stimulant use. The effect of acupuncture on treatment dropout was not significantly different between studies focusing on alcohol use and those focusing on opioid use.

No statistically significant effects were found for stimulant or cannabis use outcomes, with few statistically significant effects for alcohol or opiate use outcomes. Regarding alcohol use, there was a medium effect in favor of auricular acupuncture as an adjunct to TAU (drug therapy and psychosocial intervention), versus sham acupuncture as an adjunct to TAU, on frequency of alcohol use at six-month follow-up, though this is based on very low quality evidence from one RCT (SMD −0.79; CI −1.38 to −0.21). There was also very low quality evidence of a medium effect in favor of acupuncture (as an adjunctive or monotherapy) versus any comparator for treatment dropout at postintervention, with substantial heterogeneity (odds ratio [OR] 0.34; CI 0.12 to 0.99; $I^2$ 71.1%; 8 RCTs). Regarding opioid use, there was low quality evidence of a large effect in favor of acupuncture (as an adjunctive or monotherapy) versus any comparator for anxiety at postintervention (SMD −0.80; CI −1.30 to −0.29; $I^2$ 29.1%; 4 RCTs). There was also a medium clinical effect for withdrawal/craving at three-month follow-up in favor of auricular acupuncture (with electrostimulation) as an adjunct to a psychosocial intervention TAU versus drug therapy as an adjunct to TAU, though this was based on very low quality evidence from one RCT (SMD −0.58; CI −1.05 to −0.12).

### *Key Question 1b*

There was a diversity of acupuncture interventions. Of the 32 RCTs that provided data on auricular acupuncture, 12 specifically referred to following the National Acupuncture Detoxification Association (NADA) protocol for auricular acupuncture. Nine RCTs evaluated Traditional Chinese Medicine (TCM) acupuncture. Among all RCTs, seven involved electroacupuncture as well, including four auricular acupuncture RCTs that also provided electroacupuncture on somatic acupoints, and one auricular acupuncture RCT that involved electrostimulation of ear sites. Four RCTs provided direct comparisons of different doses of acupuncture. The length of follow-up ranged from immediately postintervention to 12 months postintervention. Acupuncture sessions ranged from 15 to 45 minutes per session, from one to 21 sessions, and for one to 32 weeks in total duration. Indirect comparisons via meta-regressions of the results of analyses by type of acupuncture yielded no statistically significant differences in effects for relapse; for withdrawal/craving symptoms and treatment dropout, TCM acupuncture studies reported more favorable effects than auricular acupuncture studies.

No consistent significant effects were found for either auricular acupuncture or TCM acupuncture on relapse, frequency of substance use, and quantity of substance use. There was a large clinical effect in favor of TCM acupuncture (as an adjunctive or monotherapy) versus any comparator for withdrawal/craving at postintervention (SMD −1.32; CI −2.12 to −0.53; $I^2$ 61.7%; 5 RCTs), though this was based on very low quality of evidence and had substantial heterogeneity. There was also a large clinical effect in favor of auricular acupuncture (with

electrostimulation) as an adjunct to psychosocial intervention TAU versus TAU alone for anxiety at postintervention (SMD −1.40; CI −2.71 to −0.08), though this is based on very low quality of evidence from one RCT. No significant effects were found for treatment dropout. There were no statistically significant differences of higher doses of acupuncture (either as more auricular points or more sessions) for relapse, treatment dropout, health-related quality of life, and functional status.

### *Key Question 1c*

Thirty-four RCTs provided data on acupuncture as an adjunctive therapy, while seven RCTs provided data on acupuncture as a monotherapy. Of the adjunctive RCTs, co-interventions involved drug therapy alone for 13 RCTs, psychosocial intervention for ten RCTs, a combination of drug therapy and psychosocial intervention for six RCTs, and one RCT each for drug therapy with a spiritual therapy, TAU with frequent urine testing, generic structured activities, drug court programming, and an undetailed usual care. Indirect comparisons of adjunctive therapy versus monotherapy via meta-regressions yielded no statistically significant differences in effects for relapse, treatment dropout, withdrawal/craving symptoms, and functional status.

We found no consistent significant effects for acupuncture as an adjunctive therapy versus any comparator (with comparators themselves as either an adjunctive therapy or as a monotherapy) for relapse, frequency of substance use, and quantity of substance use. There was very low quality evidence of a small clinical effect in favor of acupuncture as an adjunctive therapy versus all comparators for withdrawal/craving symptoms at postintervention (SMD −0.43; CI −0.79 to −0.06; $I^2$ 79.7%; 15 RCTs). No significant effect was found for health-related quality of life or functional status except a medium effect in favor of acupuncture as an adjunctive therapy versus all comparators for anxiety at postintervention (SMD −0.78; CI −1.42 to −0.15; $I^2$ 32%; 4 RCTs). No significant effect was found for treatment dropout. There were no statistically significant effects for any outcomes when analyzing those studies evaluating acupuncture as an adjunctive therapy to a comparator that is also an adjunctive therapy; there were also no significant effects from those studies with a monotherapy comparator.

No consistent significant effects for acupuncture as a monotherapy were found for relapse, withdrawal/craving symptoms, functional status (anxiety), and treatment dropout.

### *Key Question 1d*

Seven RCTs provided data on acupuncture plus TAU versus TAU alone, 19 RCTs provided data on acupuncture versus sham acupuncture, seven RCTs provided data on acupuncture versus a passive comparator, and 16 RCTs provided data on acupuncture versus an active comparator. Subgroup analyses within each type of comparator yielded no significant effects via pooled analyses. Indirect comparisons via meta-regressions of the results of analyses by type of comparator yielded no statistically significant differences in effects for relapse, treatment dropout, withdrawal/craving symptoms, and functional status.

## Conclusions

The available evidence is consistent with several previous systematic reviews that found no consistent effect of acupuncture versus comparator interventions on substance use outcomes. There were some positive effects for withdrawal symptoms and anxiety, yet these results were based on low or very low quality of evidence. The limited available evidence on adverse events suggests that acupuncture is not typically associated with serious adverse events, though some participants may experience slight bleeding/pain at the needle insertion site. Given the quality of evidence, there is uncertainty with regard to the magnitude or stability of effect estimates.

# Acknowledgments

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# Abbreviations

| | |
|---|---|
| AIDS | acquired immunodeficiency syndrome |
| AMED | Allied and Complementary Medicine Database |
| CENTRAL | Cochrane Central Register of Controlled Trials |
| CI | confidence interval |
| CINAHL | Cumulative Index to Nursing and Allied Health Literature |
| DSM | *Diagnostic and Statistical Manual of Mental Disorders* |
| GRADE | Grades of Recommendation, Assessment, Development and Evaluation |
| HIV | human immunodeficiency virus |
| ICD | International Classification of Diseases |
| ITT | intention-to-treat |
| KQ | key question |
| MANTIS | Manual, Alternative, and Natural Therapy Index System |
| MMT | methadone maintenance treatment |
| NADA | National Acupuncture Detoxification Association |
| OR | odds ratio |
| RCT | randomized controlled trial |
| SD | standard deviation |
| SMD | standardized mean difference |
| SUD | substance use disorder |
| TAU | treatment as usual |
| TCM | Traditional Chinese Medicine |

# Chapter One: Introduction

## Description of the Condition

Substance use disorders (SUDs) involving alcohol and illicit drugs are prevalent conditions among U.S. adults. Estimates of lifetime prevalence rates for substance abuse range from 13 to 18 percent for alcohol and roughly 8 percent for illicit drugs, and estimates of lifetime prevalence for dependence range from 5 to 13 percent for alcohol and roughly 3 percent for illicit drugs (Compton et al., 2007; Grant et al., 2004; Hasin et al., 2007; Kessler et al., 2005). Furthermore, 12-month prevalence rates of SUDs—either abuse or dependence—for either alcohol or illicit drugs are estimated to be 20 percent for adults aged 18–25 and 7 percent for adults aged 25 or older (Substance Abuse and Mental Health Services Administration, 2011). SUDs can lead to significant medical, social, and economic consequences, such as increasing risk of various physical illnesses, relationship issues, lost productivity, and larger health care costs (National Institute on Drug Abuse, 2008).

SUDs remain a key issue for military personnel and veteran populations. Across all services, it is estimated that 11.3 percent of active duty military personnel are problem drinkers and 1.4 percent are active users of illicit drugs (Barlas et al., 2013). Substance use by veterans appears to have risen since the start of armed conflict in Afghanistan and Iraq, with estimates of U.S. veterans with current SUDs as high as 18 percent (Golub et al., 2013; Wagner et al., 2007). While estimates of substance use among active duty military personnel are comparable to civilian populations, the prevalence of SUDs among U.S. veterans may be almost five times the rate for the general population (Substance Abuse and Mental Health Services Administration, 2007). Consequently, it is important for the Military Health System and the Veterans Health Administration to plan appropriate SUD care for their populations.

Several evidence-based pharmacological, psychological, and psychosocial interventions exist to treat and manage these disorders and their negative consequences (CASAColumbia, 2012a). However, these interventions vary in their effectiveness, safety, and acceptability to different populations, and more than 20 million Americans in need of treatment do not actually receive it (CASAColumbia, 2012b). As such, the SUD treatment community needs to investigate a variety of modalities so that treatment can best be tailored to participants' specific characteristics, disease history, and preferences.

## Description of the Intervention

Needle acupuncture is one such modality for the treatment of SUDs that has significantly increased in recent decades (Lu et al., 2009). Needle acupuncture generally involves inserting and manipulating thin solid needles into specific documented acupuncture points on the body in

order to create a therapeutic impact on bodily organs, systems, and functions—for example, by helping balance dopamine levels that are thought to influence cocaine, heroin, morphine, and alcohol use (Lua and Talib, 2012). Needle acupuncture has become a particularly prominent treatment for acupuncture due to the protocol of the National Acupuncture Detoxification Association (NADA); this protocol involves bilateral needle acupuncture of one to five specific ear points (i.e., kidney, liver, lung, Shen Men, and sympathetic) for 35- to 45-minute sessions in a group setting (Gates, Smith, and Foxcroft, 2006; Mills et al., 2005). Needle acupuncture is thought to provide a safe, simple, and inexpensive alternative to traditional treatments for preventing substance use relapse, minimizing side effects associated with conventional treatments, and increasing the availability of treatments for SUDs (Lin, Chan, and Chen, 2012).

There are several challenges to consider when conducting randomized controlled trials (RCTs) or systematic reviews on the efficacy and safety of needle acupuncture. First, authors typically do not adequately report all details of acupuncture and comparator procedures in RCTs, and reporting guidelines for acupuncture RCTs—such as the Standards for Reporting Interventions in Controlled Trials of Acupuncture recommendations—do not seem to have made an impact in improving reporting details specific to acupuncture interventions (MacPherson et al., 2002; Prady et al., 2008). In addition, methodological reviews have indicated that certain geographical regions—namely, East Asia—publish unusually high proportions of RCTs that have results in favor of acupuncture, with publication bias as a possible explanation for this pattern (Vickers et al., 1998). The choice of an appropriate comparator in acupuncture RCTs is also a key issue to consider. For example, there is considerable debate on whether sham acupuncture at acupoints that are thought to be nonspecific to SUDs, as well as superficial insertion of needles at acupoints specific to SUDs, may actually have positive effects and thus serve as inappropriate "placebo" comparators (Lua and Talib, 2012; Mills et al., 2005). A related concern is the expectancy effect of acupuncture—namely, that participants' positive expectations about the outcomes of acupuncture may be responsible in part for changes in outcomes postintervention (Mao et al., 2007).

## Why It Is Important to Do This Review

Numerous RCTs have been conducted to assess the efficacy and safety of various types of needle acupuncture used adjunctively or as monotherapy for different SUDs. However, previous reviews have concluded that more high-quality trials are needed to determine the efficacy of needle acupuncture for alcohol dependence, opiate withdrawal and addiction, cocaine addiction, and drug use generally (Cho and Whang, 2009; Gates, Smith, and Foxcroft, 2006; Jordan, 2006; Kim et al., 2006; Lin, Chan, and Chen, 2012; Liu et al., 2009; Lua and Talib, 2012; Mills et al., 2005). However, no study to date has systematically reviewed all RCTs of needle acupuncture for SUDs generally.

## Objective

This review aims to synthesize evidence from RCTs of needle acupuncture in order to provide reliable estimates of the effectiveness and safety of needle acupuncture for SUDs.

# Chapter Two: Methods

## Key Questions

We conducted a systematic review to identify RCTs testing the efficacy and safety of needle acupuncture in treating individuals with SUDs (PROSPERO record CRD42015016040). Specifically, the following key questions (KQs) guided this systematic review:

- *KQ 1*: What are the efficacy and safety of needle acupuncture, as an adjunctive or monotherapy, in reducing the frequency and quantity of substance use, withdrawal symptoms, treatment dropout, relapse, functional status, and quality of life in adults with alcohol, opioid, stimulant, or cannabis use disorders compared with active treatments, sham acupuncture, treatment as usual (TAU), wait lists, or no treatment?
  - *KQ 1a*: Does the effect of needle acupuncture vary by the substance targeted (i.e., alcohol, opioids, stimulants, or cannabis)?
  - *KQ 1b*: Is one type of needle acupuncture (e.g., auricular acupuncture) more effective than others?
  - *KQ 1c*: Is needle acupuncture more effective as an adjunctive therapy than as a monotherapy?
  - *KQ 1d*: Does the effect of needle acupuncture on SUDs depend on the comparator?

## Search Strategy

We conducted a systematic search of electronic databases (PubMed, PsycINFO, CINAHL, AMED, CENTRAL, MANTIS, and Embase; see Appendix A) from their inception to November 2014. Databases not unique to acupuncture, particularly PubMed, have preferable indexing and search features and adequate coverage of the acupuncture literature, whereas databases specific to complementary and alternative medicine (AMED, MANTIS) can be useful in identifying acupuncture RCTs not contained in these databases (Cogo et al., 2011). We decided to search databases from their inception rather than a later date because no previous systematic reviews adequately overlap our research questions, and thus we would capture all intervention studies of interest to this review. We have restricted our search to English-language publications indexed in international databases due to resource constraints, as well as the abovementioned concerns raised in the scientific literature that acupuncture trials from certain regions are likely to be proportionally high in publication bias (Vickers et al., 1998; prior unpublished RAND research). Several reviews have found that excluding trials published in languages other than English generally has little impact on summary effect estimates (Jüni et al., 2002; Moher et al., 2000), and individual review teams can consider such limits with justification.

The chief reference librarian for RAND's Knowledge Services developed the search strings for each database, informed by search results of an environmental scan of the literature at the

initiation of this study (as part of unpublished RAND research by Melony Sorbero, Sean Grant, and Susanne Hempel), as well as by the search strings of previous reviews (Cho and Whang, 2009; Gates, Smith, and Foxcroft, 2006; Jordan, 2006; Kim et al., 2006; Lin, Chan and Chen, 2012; Liu et al., 2009; Lua and Talib, 2012; Mills et al., 2005) and an unpublished RAND review on the effectiveness of acupuncture to treat posttraumatic stress disorder from the first year of this project.

## Eligibility Criteria

Inclusion and exclusion criteria for this review were developed using the framework of participants, interventions, comparators, outcomes, timing, settings, and study design, or PICOTSS:

- *Participants*: Studies were limited to adults, male and female, who are 18 years of age or older. Participants must have been diagnosed with alcohol, opioid, stimulant, and/or cannabis use disorder; diagnoses include abuse or dependence using *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-IV criteria, SUD using DSM-V criteria, or harmful use or dependence syndrome using International Classification of Diseases (ICD) criteria.
- *Interventions*: Studies that administered thin or fine solid needles into known acupuncture points, either as an adjunctive or monotherapy, were included. Studies involving full-body acupuncture, auricular acupuncture, or other specific body sites, with or without electrostimulation, were included. Studies involving acupuncture via laser, heat, or light were excluded, unless needles were also used. Studies involving dry needling or trigger point and not referring to traditional acupuncture were excluded.
- *Comparators*: Studies that included sham acupuncture, TAU or "standard care," passive comparators (e.g., wait-list control, no treatment), or other active treatments were included.
- *Outcomes*: Studies that reported one or more of the following outcomes were included: frequency of substance use, quantity of substance use, withdrawal symptoms, treatment dropout, relapse, functional status, health-related quality of life, and adverse events.
- *Timing*: Studies could have involved any treatment duration and follow-up period.
- *Setting*: Studies were not limited by setting (e.g., country, physical location of treatment).
- *Study design*: Included studies were limited to parallel group trials or controlled trials that were individually randomized or cluster-randomized. Data reported only in conference proceedings or abstracts were excluded.

## Inclusion Screening

Two independent reviewers from RAND (the project lead, who is a doctoral-level experienced systematic reviewer, and a RAND research assistant with experience in systematic reviews) screened titles and abstracts of retrieved citations. An initial session piloting the screening form occurred prior to these reviews to ensure similar interpretation of the inclusion and exclusion criteria. Citations judged as potentially eligible by one or both reviewers were

obtained as full text. The full-text publications were then screened against the specified inclusion criteria by the two independent reviewers; any disagreements were resolved through discussion within the review author team.

## Data Extraction

The two aforementioned reviewers each independently abstracted study-level data in an electronic database. The project lead designed data collection forms with input from the project team. The two reviewers pilot-tested the data collection forms on a few well-reported studies to ensure agreement of interpretation. The project lead abstracted all outcome data. The analyses were performed by a biostatistician and a methodologist at the RAND Evidence-based Practice Center.

The following information was abstracted from each study:

- *Participants*: gender, age, and baseline substance use
- *Interventions*: type of needle acupuncture (whole body, microsystem acupuncture, acupoints), dosage (intensity, frequency, duration), and co-intervention(s)
- *Comparators*: type of comparator
- *Outcomes assessed*: frequency and quantity of substance use, withdrawal or craving symptoms, treatment dropout, relapse, functional status, health-related quality of life, and adverse events; for each of these outcomes, we abstracted data on domain (e.g., frequency of substance use), method of measurement (e.g., Time Line Follow Back), Metric Of Data Expression (E.G., Means, Proportions), Primary Endpoint (e.g., six-month follow-up), and corresponding results (i.e., effect estimate, precision)
- *Timing*: time-points of outcome assessment and timing of intervention administration (e.g., residential care, outpatient)
- *Setting*: geographic region, type of health care setting (general health care setting versus specialty SUD care), and number of sites
- *Study design*: aim of study, inclusion and exclusion criteria, sample size, reported power calculations, and items relevant to risk of bias and quality ratings.

When several reports for the same study existed, we compared descriptions of participants to ensure that data from the same study populations entered analysis and synthesis only once. This situation occurred for six studies (see Appendix B).

## Risk of Bias

The two reviewers assessed the risk of bias of included studies using the Cochrane Risk of Bias tool (Higgins et al., 2011). Specifically, the reviewers assessed risks of bias related to the following domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and providers (performance bias), blinding of outcome assessors (detection bias), completeness of reporting outcome data (attrition bias), and selective

outcome reporting (reporting bias). Please see Appendix C for an overview of the criteria used to make risk-of-bias determinations.

Other biases related to the U.S. Preventive Services Task Force's (2008) criteria for internal validity of included studies were also assessed, namely those related to equal distribution among groups of potential confounders at baseline; cross-overs or contamination between groups; equal, reliable, and valid outcome measurement; clear definitions of interventions; and intention-to-treat analysis. These criteria were used to rate the quality of evidence of individual included studies using the following guidelines (Lewin Group and ECRI Institute, 2014; U.S. Preventive Services Task Force, 2008):

- *Good*: Comparable groups are initially assembled and maintained throughout the study with at least 80-percent follow-up; reliable, valid measurement is used and applied equally to all groups; interventions are clearly described; all important outcomes are considered; appropriate attention is given to confounders in analysis; intention-to-treat analysis is used.
- *Fair*: One or more of the following issues is found in the study: some though not major differences between groups exist at follow-up; measurement instruments are acceptable but not ideal, though are generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for in analyses. In addition, intention-to-treat analysis must be done.
- *Poor*: One or more of the following "fatal flaws" is found in the study: initially assembled groups are not comparable or maintained throughout the study; unreliable or invalid measurements are used or applied unequally across groups; key confounders are given little to no attention in analyses; intention-to-treat analysis is not used.

## Data Synthesis

The primary aim of this systematic review is to identify whether needle acupuncture is effective in reducing frequency and quantity of substance use, withdrawal symptoms, treatment dropout, relapse, and adverse events, as well as in improving functional status and health-related quality of life, in adults with SUDs. Therefore, when sufficient data were available, we performed random-effects meta-analyses to pool effectiveness results across included studies for the outcomes of interest. Forest plots for main outcomes are provided in this report for meta-analyses pooling at least three studies. For some outcomes (e.g., relapse), we combined dichotomous and continuous outcomes to maximize the number of studies available per analysis. We used the Hartung-Knapp-Sidik-Jonkman method for our random-effects meta-analysis (Hartung, 1999; Hartung and Knapp, 2001; Sidik and Jonkman, 2006). This method may be preferred when the number of studies pooled is small and when there is evidence of heterogeneity (IntHout, Ioannidis, and Borm, 2014). It has been shown that the error rates are more robust than the previously used DerSimonian and Laird method (Sánchez-Meca and Marín-Martínez, 2008).

Outcomes were grouped by length of follow-up (0–2 months for postintervention, 3–12 months for short-term follow-up). Tests of heterogeneity were performed using the $I^2$ statistic. Values of the $I^2$ statistic closer to 100 percent represent higher degrees of heterogeneity, with an $I^2$ of 30 percent to 60 percent possibly representing moderate heterogeneity, 50 percent to 90 percent substantial heterogeneity, and 75 percent to 100 percent considerable heterogeneity (Higgins et al., 2003). Common indices for interpreting the size of clinical effects were used: standardized mean difference (SMD) of 0.2 or odds ratio (OR) of 0.60 for a small clinical effect; SMD of 0.5 or OR of 0.29 for a medium clinical effect; and SMD of 0.8 or OR of 0.15 for a large clinical effect (Chen, Cohen, and Chen, 2010).

In addition, when sufficient data were available, we conducted subgroup analyses and meta-regressions to address secondary aims of this systematic review. Specifically, we examined whether there were differences in effect sizes between studies conducted in different groups—namely, by type of substance use (i.e., alcohol, opioid, stimulant, or cannabis), by type of needle acupunctures (e.g., auricular acupuncture), as a monotherapy versus an adjunctive therapy, and by type of comparison group in the trial. In order to conduct meta-regressions, each subgroup had to contain at least two unique studies, and no one study could be in more than one subgroup in the same meta-regression. In order to prevent overlap of data between subgroups, studies that could fall into multiple subgroups within one meta-regression (e.g., a three-arm trial with two different comparison groups) were assigned to the subgroup with the least amount of data (e.g., the comparison group with the fewest studies).

For meta-analysis of data with clear outliers, sensitivity analyses were *a priori* planned to be conducted (excluding the outliers), if appropriate (Greenland and Longnecker, 1992; Orsini et al., 2012; Hamling et al., 2008; Higgins et al., 2011). No such sensitivity analyses were undertaken. Although we designed our search strategy to exclude acupuncture literature with suspected publication biases, we also investigated publication bias for all main analyses with sufficient data using Begg's rank correlation test for funnel plot asymmetry (Begg and Mazumdar, 1994) and Egger's test for funnel plot asymmetry (Egger et al., 1997).

## Quality of Evidence

The quality of evidence was assessed for major outcomes using the Grades of Recommendation, Assessment, Development, and Evaluation (or GRADE) approach (Berkman et al., 2014; Lewin Group and ECRI Institute, 2014). Namely, the body of evidence was assessed based on the following dimensions: study limitations (low, medium, or high), directness (direct or indirect), consistency (consistent, inconsistent, or unknown), and precision (precise or imprecise) (Egger et al., 1997). For this review, we assessed study limitations, via the risk of bias assessments detailed above; directness, via how well various aspects of studies (e.g., population, intervention, comparator) address this review's key questions; consistency, via the magnitude of

heterogeneity; and precision, via the width of confidence intervals. The quality of evidence was graded on the following four-item scale:

- *High* indicates that the review authors are very confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has few or no deficiencies. As such, the reviewers believe the findings are stable. That is, further research is very unlikely to change confidence in the effect estimate.
- *Moderate* indicates that the review authors are moderately confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has some deficiencies. As such, the reviewers believe that the findings are likely to be stable, but further research may change confidence in the effect estimate and may even change the estimate.
- *Low* indicates that the review authors have limited confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has major or numerous (or both) deficiencies. As such, the reviewers believe that additional evidence is needed before concluding either that the findings are stable or that the effect estimate lies close to the true effect.
- *Very low* indicates that the review authors have very little confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has very major deficiencies. As such, the true effect is likely to be substantially different from the estimated effect; thus, any estimate of effect is very uncertain.

# Chapter Three: Results

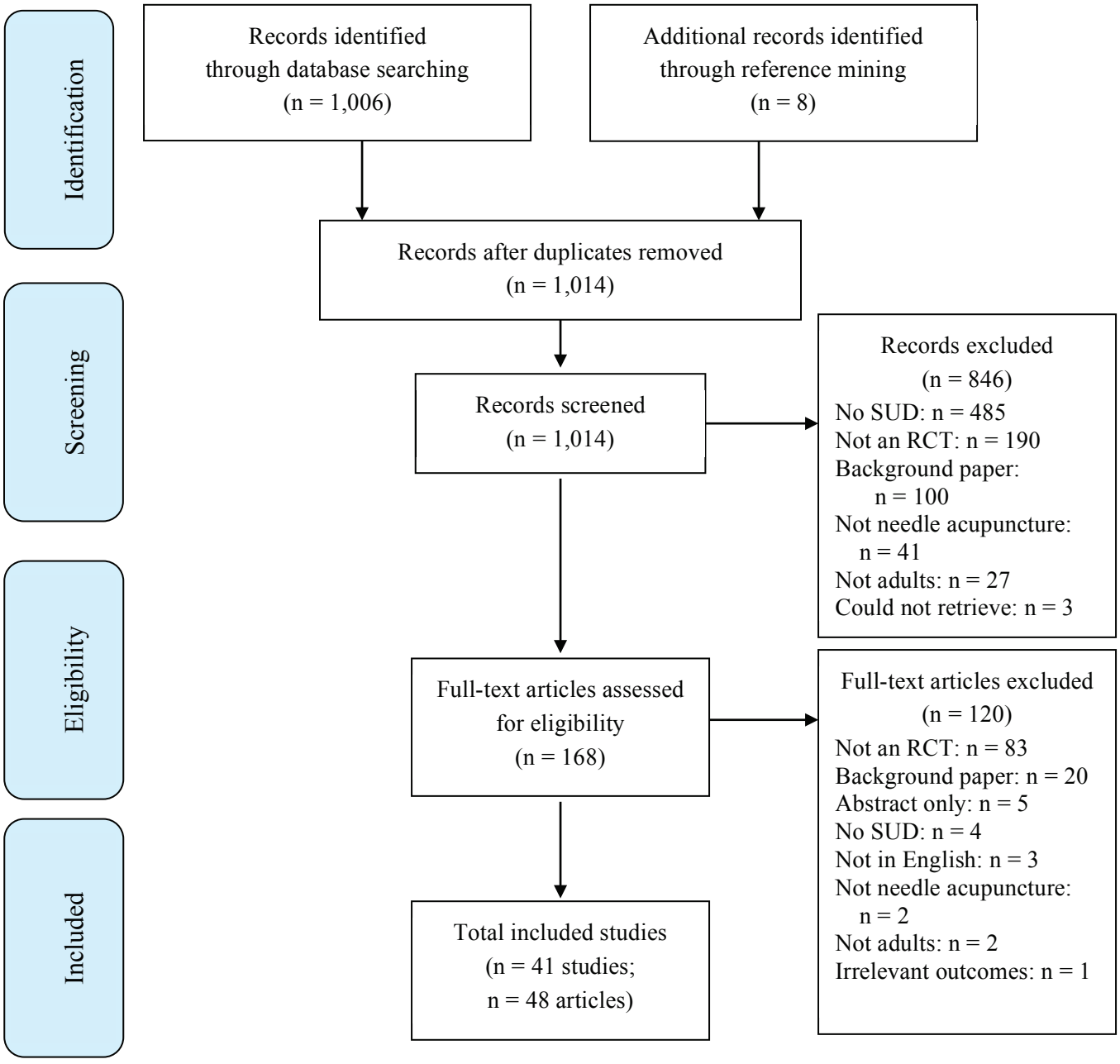
## Results of the Search

We identified 1,006 records through our electronic search of databases, plus eight records through reference mining of included studies and 18 previous reviews related to needle acupuncture. After deduplication, we examined 1,014 titles and abstracts (see Figure 3.1).

Full texts were obtained for 168 records identified as potentially eligible by the two reviewers. Of these, 120 articles were excluded at the full-text review, either because they did not involve a parallel group RCT (n = 83), were conference abstracts with no results published (n = 5), were background review articles (n = 20), did not involve participants with eligible SUD diagnoses (n = 4), were not published in English (n = 3), did not involve needle acupuncture (n = 2), did not involve adult populations (n = 2), or focused on irrelevant outcomes such as brain activity (n = 1). A list of studies excluded at the full-text review is shown in Appendix D.

Two studies required review team discussion regarding eligibility, both of which were ultimately excluded. One of these studies (Margolin, Avants, et al., 1996) was a within-subjects trial that randomized different ears of the same participants to either auricular acupuncture or sham acupuncture, in order to define points for needle insertion prior to a multisite RCT of auricular acupuncture for cocaine addiction. The other study (Berman et al., 2004) was excluded because "drug of preference" was the only information provided about participants' substance use; the review team agreed that there was insufficient information provided in the report to confirm that the RCT participants had a diagnosis of substance abuse or dependence.

**Figure 3.1. Flow Diagram of Search Results**




Overall, we identified 41 eligible studies, reported across 48 articles. Of these, 41 RCTs provided data on the efficacy of needle acupuncture, and 12 RCTs provided data on the safety of needle acupuncture (see Table 3.1 for the evidence base for this study's key questions).

**Table 3.1. Evidence Base for Key Questions**

| Key Question | | Number of RCTs |
|---|---|---|
| KQ 1 | What are the efficacy and safety of needle acupuncture, as an adjunctive or monotherapy, in reducing the frequency and quantity of substance use, withdrawal symptoms, treatment dropout, and relapse in adults with alcohol, opioid, stimulant, or cannabis use disorders compared with active treatments, sham acupuncture, TAU, wait lists, or no treatment? | 41 RCTs with efficacy data- |
| | | 12 RCTs with safety data |
| KQ 1a | Does the effect of needle acupuncture vary by the substance targeted (i.e., alcohol, opioids, stimulants, or cannabis)? | 11 alcohol RCTs |
| | | 13 opioids RCTs |
| | | 10 stimulants RCTs |
| | | 1 cannabis RCT |
| KQ 1b | Is one type of needle acupuncture (e.g., auricular acupuncture) more effective than others? | 32 auricular acupuncture RCTs |
| | | 9 Traditional Chinese Medicine (TCM) acupuncture RCTs |
| | | 7 RCTs with electroacupuncture |
| | | 4 RCTs with different acupuncture doses |
| KQ 1c | Is needle acupuncture more effective as an adjunctive therapy than as a monotherapy? | 34 adjunctive therapy RCTs |
| | | 7 monotherapy RCTs |
| KQ 1d | Does the effect of needle acupuncture on SUDs depend on the comparator? | 7 acupuncture + TAU versus TAU RCTs |
| | | 19 sham acupuncture RCTs |
| | | 7 passive comparator RCTs |
| | | 15 active comparator RCTs |

For KQ 1, we identified 12 RCTs with safety data (Avants, Margolin, Holford, et al., 2000; Bullock, Kiresuck, Sherman, et al., 2002; Chang, Sommers, and Herz, 2010; Chan et al., 2014; Kunz et al., 2007; Lee et al., 2014; Lua and Talib, 2013; Otto, Quinn, and Sung, 1998; Rampes et al., 1997; Trumpler et al., 2003; Washburn et al., 1993).

For KQ 1a on the effect of needle acupuncture by substance targeted, we identified 11 RCTs on alcohol use specifically (Bullock, Umen, et al., 1987; Bullock, Culliton, and Olander, 1989; Kunz et al., 2007; Bullock, Kiresuck, Sherman, et al., 2002; Karst et al., 2002; Lee et al., 2014; Rampes et al., 1997; Sapir-Weise et al., 1999; Toteva and Milanov, 1996; Trumpler et al., 2003; Worner et al., 1992); ten RCTs on stimulant use specifically (Margolin, Kleber, et al., 2002; Avants, Margolin, Chang, et al., 1995; Avants, Margolin, Holford, et al., 2000; Bullock, Kiresuk, Pheley, et al., 1999a and 1999b [Note: There were two studies included in Bullock, Kiresuk, Pheley, et al., 1999; we note them as 1999a and 1999b. See Appendix B for details of each study.]; Killeen et al., 2002; Konefal, Duncan, and Clemence, 1994; Lipton, Brewington, and Smith, 1994; Otto, Quinn, and Sung, 1998; Richard et al., 1995); 13 RCTs on opioid use specifically (Bearn et al., 2009; Chan et al., 2014; Leung, 1977; Liang et al., 2012; Lua and Talib, 2013; Montazeri, Farahnakian, and Saghaei, 2002; Mu et al., 2013; Pirmoradi and

Abdollahi, 2008; Song, Hu, et al., 2010; Song, Li, et al., 2012; Washburn et al., 1993; Wells et al., 1995; Zeng et al., 2005); and one RCT on cannabis use specifically (Konefal, Duncan, and Clemence, 1994).

For KQ 1b on the effect of needle acupuncture by type of acupuncture, we identified 32 RCTs evaluating auricular acupuncture (Avants, Margolin, Chang, et al., 1995; Avants, Margolin, Holford, et al., 2000; Bearn et al., 2009; Black et al., 2011; Bullock, Kiresuk, Pheley, et al., 1999a and 1999b; Bullock, Umen, et al., 1987; Bullock, Culliton, and Olander, 1989; Bullock, Kiresuck, Sherman, et al., 2002; Chan et al., 2014; Chang, Sommers, and Herz, 2010; Janssen et al., 2012; Karst et al., 2002; Killeen et al., 2002; Konefal, Duncan, and Clemence, 1994; Konefal, Duncan, and Clemence, 1995; Kunz et al., 2007; Leung, 1977; Lipton, Brewington, and Smith, 1994; Lua and Talib, 2013; Man and Chuang, 1980; Margolin, Kleber, et al., 2002; Margolin, Avants, and Arnold, 2005; Pirmoradi and Abdollahi, 2008; Rampes et al., 1997; Richard et al., 1995; Sapir-Weise et al., 1999; Trumpler et al., 2003; Washburn et al., 1993; Wells et al., 1995; White, Goldkamp, and Robinson, 2006); nine RCTs evaluating Traditional Chinese Medicine (TCM) acupuncture (Lee et al., 2014; Liang et al., 2012; Montazeri, Farahnakian, and Saghaei, 2002; Mu et al., 2013; Song, Hu, et al., 2010; Song, Li, et al., 2012; Toteva and Milanov, 1996; Worner et al., 1992; Zeng et al., 2005); seven RCTs involving electroacupuncture (Chan et al., 2014; Leung, 1977; Mu et al., 2013; Pirmoradi and Abdollahi, 2008; Rampes et al., 1997; Toteva and Milanov, 1996; Zeng et al., 2005); and four RCTs involving evaluations of different doses of needle acupuncture (Bullock, Kiresuk, Pheley, et al., 1999b; Konefal, Duncan, and Clemence, 1995; Margolin, Avants, and Arnold, 2005; Bullock, Kiresuck, Sherman, et al., 2002).

For KQ 1c on the effect of needle acupuncture as an adjunctive versus a monotherapy, we identified 34 RCTs evaluating acupuncture as an adjunctive therapy (Avants, Margolin, Chang, et al., 1995; Avants, Margolin, Holford, et al., 2000; Bearn et al., 2009; Black et al., 2011; Bullock, Kiresuk, Pheley, et al., 1999a and 1999b; Bullock, Culliton, and Olander, 1989; Bullock, Kiresuck, Sherman, et al., 2002; Chan et al., 2014; Chang, Sommers, and Herz, 2010; Janssen et al., 2012; Karst et al., 2002; Konefal, Duncan, and Clemence, 1994; Konefal, Duncan, and Clemence, 1995; Kunz et al., 2007; Lee et al., 2014; Lua and Talib, 2013; Man and Chuang, 1980; Margolin, Kleber, et al., 2002; Margolin, Avants, and Arnold, 2005; Montazeri, Farahnakian, and Saghaei, 2002; Mu et al., 2013; Otto, Quinn, and Sung, 1998; Pirmoradi and Abdollahi, 2008; Rampes et al., 1997; Richard et al., 1995; Sapir-Weise et al., 1999; Song, Hu, et al., 2010; Trumpler et al., 2003; Washburn et al., 1993; Wells et al., 1995; White, Goldkamp, and Robinson, 2006; Worner et al., 1992; Zeng et al., 2005); and seven RCTs evaluating acupuncture as a monotherapy (Bullock, Umen, et al., 1987; Killeen et al., 2002; Leung, 1977; Liang et al., 2012; Lipton, Brewington, and Smith, 1994; Song, Li, et al., 2012; Toteva and Milanov, 1996).

For KQ 1d on the effect of needle acupuncture dependent on type of comparator, we identified seven RCTs evaluating acupuncture plus TAU versus TAU alone (Bullock, Kiresuk,

Pheley, et al., 1999a; Bullock, Kiresuck, Sherman, et al., 2002; Chang, Sommers, and Herz, 2010; Konefal, Duncan, and Clemence, 1994; Rampes et al., 1997; Richard et al., 1995; Worner et al., 1992); no RCTs evaluating acupuncture versus TAU; 19 RCTs evaluating acupuncture versus sham acupuncture (Avants, Margolin, Chang, et al., 1995; Avants, Margolin, Holford, et al., 2000; Bearn et al., 2009; Black et al., 2011; Bullock, Kiresuk, Pheley, et al., 1999a; Bullock, Umen, et al., 1987; Bullock, Culliton, and Olander, 1989; Bullock, Kiresuck, Sherman, et al., 2002; Chan et al., 2014; Karst et al., 2002; Killeen et al., 2002; Lee et al., 2014; Leung, 1977; Lipton, Brewington, and Smith, 1994; Margolin, Kleber, et al., 2002; Otto, Quinn, and Sung, 1998; Rampes et al., 1997; Sapir-Weise et al., 1999; Washburn et al., 1993; Wells et al., 1995); seven RCTs evaluating acupuncture versus a passive control (Avants, Margolin, Holford, et al., 2000; Black et al., 2011; Liang et al., 2012; Margolin, Kleber, et al., 2002; Song, Hu, et al., 2010; Song, Li, et al., 2012; Trumpler et al., 2003); and 15 RCTs evaluating acupuncture versus an active comparator (Chang, Sommers, and Herz, 2010; Konefal, Duncan, and Clemence, 1994; Kunz et al., 2007; Pirmoradi and Abdollahi, 2008; Richard et al., 1995; Toteva and Milanov, 1996; Trumpler et al., 2003; White, Goldkamp, and Robinson, 2006; Worner et al., 1992; Janssen et al., 2012; Lu and Lu, 2013; Man and Chuang, 1980; Montazeri, Farahnakian, and Saghaei, 2002; Mu et al., 2013; Zeng et al., 2005).

## Description of Included Studies

*Design.* All RCTs randomized individual participants rather than clusters of participants (see Appendix B). Overall, studies assigned 5,227 participants, ranging in size from 17 participants (Leung, 1977) to 620 (Margolin, Kleber, et al., 2002), with a median sample size of 72 participants per study. Twenty-nine studies did not report any information about a power calculation, ten studies reported an *a priori* power calculation with targeted sample size achieved, and two studies noted a post hoc analysis indicating insufficient power (Avants, Margolin, Chang, et al., 1995; Janssen et al., 2012). Twenty-eight studies were two-arm RCTs, 11 were three-arm RCTs, and two were four-arm RCTs.

*Setting.* Studies were conducted in 12 countries: 21 studies took place in the United States; five took place in China; three took place in Canada; two studies each took place in Germany, Iran, and the United Kingdom; and one study each took place in Bulgaria, Malaysia, South Korea, Sweden, Switzerland, and Taiwan. All studies took place in SUD specialty care settings, with 20 studies taking place in outpatient settings and 21 studies in inpatient settings. Most studies took place at one site, though one study took place at two sites (Wells et al., 1995), three studies took place at three sites (Black et al., 2011; Lua and Talib, 2013; Man and Chuang, 1980), and one study took place at six sites (Margolin, Kleber, et al., 2002).

*Participants.* Average age ranged from 28 to 45 years. One RCT had only females (Janssen et al., 2012), and ten RCTs had only males (Bullock, Umen, et al., 1987; Chang, Sommers, and Herz, 2010; Lee et al., 2014; Liang et al., 2012; Lua and Talib, 2013; Man and Chuang, 1980;

Montazeri, Farahnakian, and Saghaei, 2002; Otto, Quinn, and Sung, 1998; Song, Hu, et al., 2010; Song, Li, et al., 2012); of the remaining RCTs, the proportion of males ranged from 50 to 94 percent.

*Interventions.* Acupuncture sessions ranged from 15 to 45 minutes per session, from one to 21 sessions, and for one to 32 weeks in total duration. Of the 32 RCTs that provided data on auricular acupuncture, 12 RCTs specifically referred to following the NADA protocol (Avants, Margolin, Holford, et al., 2000; Bearn et al., 2009; Black et al., 2011; Chang, Sommers, and Herz, 2010; Janssen et al., 2012; Killeen et al., 2002; Konefal, Duncan, and Clemence, 1994; Konefal, Duncan, and Clemence, 1995; Kunz et al., 2007; Lua and Talib, 2013; Margolin, Avants, and Arnold, 2005; Margolin, Kleber, et al., 2002). Nine RCTs evaluated TCM acupuncture, varying with regards to session length and frequency, as well as acupoints used. Two of the TCM acupuncture RCTs applied moxibustion (Song, Hu, et al., 2010; Song, Li, et al., 2012) to enhance needle acupuncture. Seven RCTs also involved electroacupuncture (i.e., electrostimulation of needles), of which four auricular acupuncture RCTs also provided electroacupuncture on somatic acupoints and one auricular acupuncture RCT involved electrostimulation of ear sites.

*Comparators.* Seven RCTs provided data on acupuncture plus TAU versus TAU alone; all TAUs involved psychosocial interventions. There were 19 sham acupuncture comparators across all RCTs: 15 involved nonspecific points that are not intended to address chemical dependency, and four involved superficial needling at points intended for chemical dependency. There were seven passive intervention comparators across all RCTs: three involved no treatment, three involved relaxing in a soothing room, and one involved a sham laser passive comparator. There were 16 active comparators from 15 RCTs: nine involved drug therapy, two involved relaxation therapy, one involved aromatherapy, one involved transdermal stimulation, one involved frequent urine testing (to promote abstention from substance use), one involved brainwave modification, and one involved laser acupuncture. In addition, four trials compared providing different doses of acupuncture, such as using 1–3 points from NADA protocol, with providing eight or 16 (rather than 28) acupuncture sessions.

*Outcomes*. Length of follow-up ranged from immediately postintervention to 12 months postintervention. The information from the studies included the following: 11 RCTs on relapse to substance use, 22 RCTs on treatment dropout, nine RCTs on withdrawal/craving symptoms, two RCTs on frequency of use, three RCTs on quantity of use, three RCTs on health-related quality of life, 11 RCTs on functional status, four RCTs on recovery outcomes, and 12 RCTs on adverse events.

## Study Quality and Risk of Bias for Individual Included Studies

The study quality and risk of bias for each of the included studies can be found in Table 3.2. Eight studies in total received a "good" quality rating, 13 were judged to be of fair quality, and 19 were judged to be of poor quality.

*Random sequence generation.* Sixteen studies had low risk of selection bias from random sequence generation, 22 had an unclear risk of bias, and three had a high risk of bias.

*Allocation concealment.* Eight studies had low risk of selection bias related to allocation concealment, 30 had an unclear risk of bias, and three had a high risk of bias.

*Blinding of participants and providers.* All studies were de facto rated high risk of performance bias related to blinding of intervention providers, because it is generally impossible for a provider to be blinded from delivery of acupuncture. One study (Lipton, Brewington, and Smith, 1994) did potentially mitigate this bias by using additional staff to ensure that the acupuncturist and participants did not communicate at all during treatment, whereas another study had a treatment protocol in place to limit interaction between the acupuncturist and participant beyond what was necessary (Margolin, Avants, and Holford, 2002; Margolin, Avants, and Kleber, 1998).

Sixteen studies had low risk of performance bias related to blinding of intervention participants, one study had an unclear risk of bias, and 20 studies had a high risk of bias. Four studies had multiple treatment arms, in which one arm received sham acupuncture and the other arm did not involve acupuncture; as a result, these studies were at low risk of performance bias for true versus sham acupuncture comparisons, and high risk of performance bias for acupuncture versus nonacupuncture comparisons.

*Blinding of outcome assessors.* Twenty-five studies had a low risk of detection bias related to blinding of outcome assessors, 13 had an unclear risk of bias, and three had a high risk of bias.

*Outcome data.* Twenty studies were at low risk of attrition biases related to missing data in the RCT, two had an unclear risk of bias, and 19 had a high risk of bias.

*Selective outcome reporting.* Two studies had a low risk of reporting bias related to subjective outcome reporting, 22 studies had an unclear risk of bias, and 17 studies had a high risk of bias.

**Table 3.2. Study Quality/Risk of Bias for Individual Included Studies**

| Study | Random Sequence Generation (selection bias) | Allocation Concealment (selection bias) | Blinding of Participants (performance bias) | Blinding of Outcome Assessors (detection bias) | Completeness of Reporting Outcome Data (attrition bias) | Selective Outcome Reporting (reporting bias) | Other Biases[b] | USPSTF Quality Rating[c] |
|---|---|---|---|---|---|---|---|---|
| Avants, Margolin, Chang, et al., 1995 | Unclear | Unclear | Low | Low | High | High | ITT analysis | Poor |
| Avants, Margolin, Holford, et al., 2000 | Low | Unclear | Low/High[a] | Low | High | Unclear | None | Good |
| Bearn et al., 2009 | Low | Unclear | Low | Unclear | Unclear | Unclear | ITT analysis | Poor |
| Black, et al., 2011 | Low | Low | Low | Low | Low | High | ITT analysis | Poor |
| Bullock, Umen, et al., 1987 | Unclear | Unclear | Low | Low | High | High | Baseline confounding unclear | Fair |
| Bullock, Culliton, and Olander, 1989 | Unclear | Unclear | Low | Low | High | Unclear | ITT analysis | Poor |
| Bullock, Kiresuk, Pheley, et al., 1999a | High | Unclear | Low/High[a] | Low | High | Unclear | ITT analysis | Poor |
| Bullock, Kiresuk, Pheley, et al., 1999b | Unclear | Unclear | High | Low | High | High | Baseline confounding unclear | Fair |
| Bullock, Kiresuck, Sherman, et al., 2002 | Unclear | Unclear | Low/High[a] | Low | Low | High | None | Fair |
| Chan et al., 2014 | Low | Low | Low | Low | Low | Low | None | Good |
| Chang, Sommers, and Herz, 2010 | Unclear | Unclear | High | High | Low | High | None | Good |
| Janssen et al., 2012 | Low | Low | High | Low | Low | Low | None | Good |
| Karst et al., 2002 | Unclear | Unclear | Low | Low | Low | Unclear | None | Good |
| Killeen et al., 2002 | Unclear | Unclear | Low | Unclear | Low | Unclear | None | Good |
| Konefal, Duncan, and Clemence, 1994 | Unclear | Unclear | High | Low | High | Unclear | ITT analysis | Poor |
| Konefal, Duncan, and Clemence, 1995 | Unclear | Unclear | High | Low | High | High | ITT analysis | Poor |
| Kunz et al., 2007 | Unclear | Unclear | High | Unclear | High | High | Baseline confounding | Fair |

| Study | Random Sequence Generation (selection bias) | Allocation Concealment (selection bias) | Blinding of Participants (performance bias) | Blinding of Outcome Assessors (detection bias) | Completeness of Reporting Outcome Data (attrition bias) | Selective Outcome Reporting (reporting bias) | Other Biases[b] | USPSTF Quality Rating[c] |
|---|---|---|---|---|---|---|---|---|
| Lee et al., 2014 | Low | Unclear | Low | Low | Low | Unclear | None | Fair |
| Leung, 1977 | Low | High | Low | Low | Low | Unclear | ITT analysis, outcome measurement, and baseline confounding are unclear | Poor |
| Liang et al., 2012 | Unclear | Unclear | High | Unclear | Low | Unclear | ITT analysis (only 3% attrition) | Fair |
| Lipton, Brewington, and Smith, 1994 | High | High | Low | Low | High | High | Baseline confounding, contamination, outcome measurement, and ITT analysis | Poor |
| Lua and Talib, 2013 | Low | Low | High | Unclear | High | Unclear | Baseline confounding, ITT analysis | Poor |
| Man and Chuang, 1980 | Unclear | Unclear | High | Low | High | High | Outcome measurement, clear intervention definition; baseline confounding, contamination, and ITT analysis are unclear | Poor |
| Margolin, Kleber, et al., 2002 | Low | Low | Low | Low | High | High | None | Fair |
| Margolin, Avants, and Arnold, 2005 | Unclear | Unclear | Unclear | Unclear | Low | Unclear | None | Good |
| Montazeri, Farahnakian, and Saghaei, 2002 | Low | Unclear | High | Low | Low | High | None | Fair |
| Mu et al., 2013 | Low | Unclear | High | Unclear | Low | Unclear | None | Fair |
| Otto, Quinn, and Sung, 1998 | Unclear | Low | Low | Low | High | High | ITT analysis | Poor |
| Pirmoradi and Abdollahi, 2008 | Unclear | Unclear | High | Unclear | Unclear | Unclear | Outcome measurement; baseline confounding and ITT analysis are unclear | Poor |
| Rampes et al., 1997 | Low | Low | Low/High[a] | Low | High | Unclear | ITT analysis | Poor |
| Richard et al., 1995 | Unclear | Unclear | High | Unclear | High | High | ITT analysis | Poor |
| Sapir-Weise et al., | Unclear | Unclear | Low | Low | Low | High | None | Fair |

| Study | Random Sequence Generation (selection bias) | Allocation Concealment (selection bias) | Blinding of Participants (performance bias) | Blinding of Outcome Assessors (detection bias) | Completeness of Reporting Outcome Data (attrition bias) | Selective Outcome Reporting (reporting bias) | Other Biases[b] | USPSTF Quality Rating[c] |
|---|---|---|---|---|---|---|---|---|
| 1999 | | | | | | | | |
| Song, Hu, et al., 2010 | Unclear | Unclear | High | Unclear | Low | Unclear | None | Fair |
| Song, Li, et al., 2012 | Low | Unclear | High | High | Low | Unclear | None | Fair |
| Toteva and Milanov, 1996 | Unclear | Unclear | High | Unclear | High | Unclear | ITT analysis; outcome measurement is unclear | Poor |
| Trumpler et al., 2003 | Low | Low | High | High | Low | Unclear | Outcome measurement | Fair |
| Washburn et al., 1993 | Unclear | Unclear | Low | Low | High | High | None | Fair |
| Wells et al., 1995 | Low | Unclear | Low | Low | High | High | ITT analysis | Poor |
| White, Goldkamp, and Robinson, 2006 | High | High | High | Unclear | Low | Unclear | Contamination | Poor |
| Worner et al., 1992 | Low | Unclear | High | Low | Low | Unclear | None | Good |
| Zeng et al., 2005 | Unclear | Unclear | High | Unclear | Low | Unclear | ITT analysis; outcome measurement is unclear | Poor |

NOTES: ITT = intention-to-treat; USPSTF = U.S. Preventive Services Task Force.
All trials were de facto "high" risk of bias for blinding of providers.
[a] Trials that had more than one comparison condition and at least one comparison condition could be considered low risk for participant blinding (e.g., sham acupuncture).
[b] Other biases include balance of confounders, crossovers/contamination, measurement, intervention definition, and intention-to-treat analysis.
[c] The USPSTF criteria (U.S. Preventive Services Task Force, 2008) for study quality involve assessment of various factors related to the internal validity of the study. "Good" is the highest ranking, which involves comparable groups with low attrition, with outcomes being reliably and validly measured and analyzed. "Fair" is the next highest rating and involves studies with one or a few potential concerns (e.g., some though not major differences between groups exist at follow-up), though intention-to-treat analysis was performed. "Poor" is the lowest ranking and involves studies with one or more "fatal flaws" (e.g., no intention-to-treat analysis).

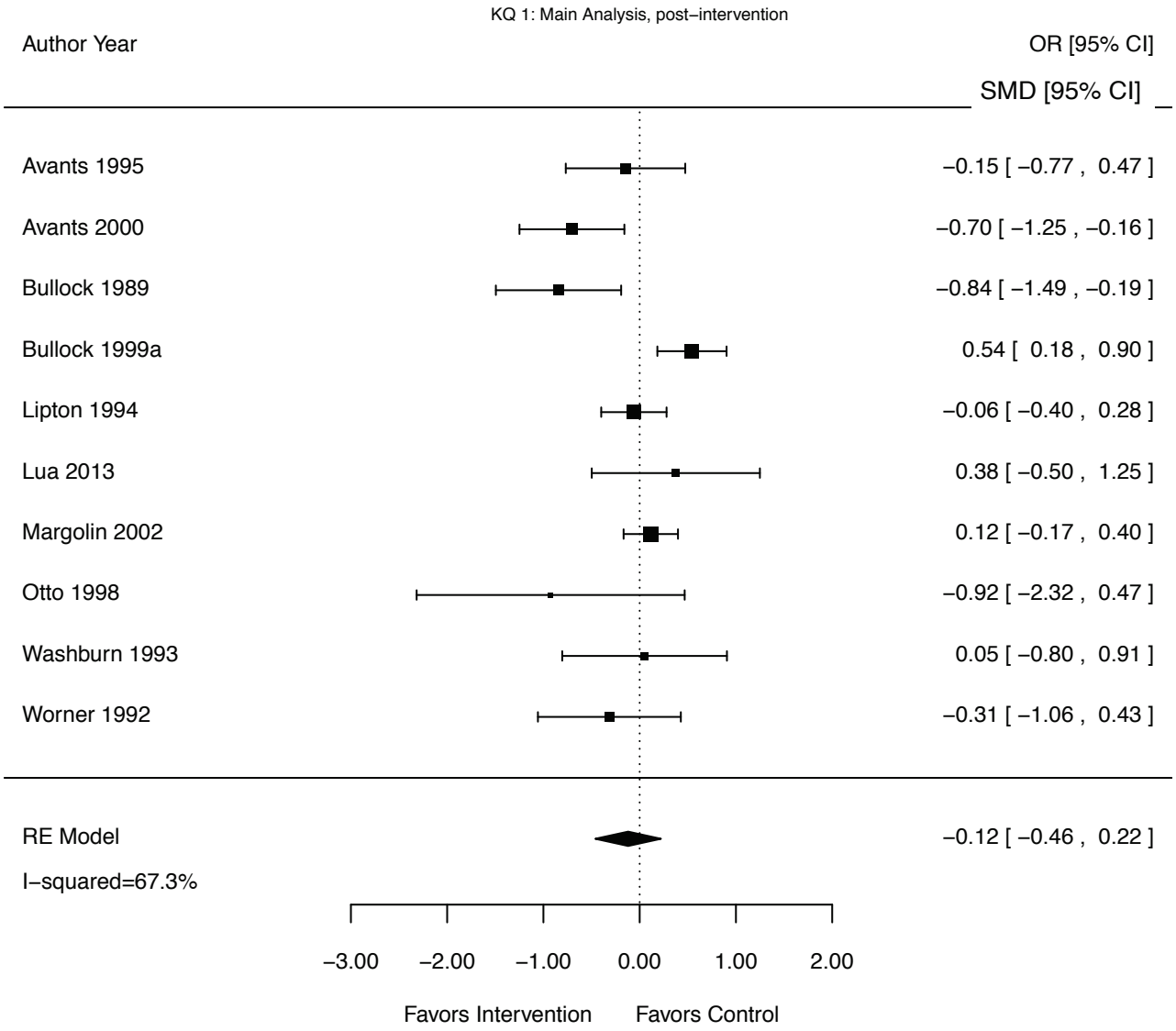
## KQ 1: What Are the Efficacy and Safety of Needle Acupuncture, as an Adjunctive or Monotherapy, for SUDs Versus Any Comparator?

We identified 41 RCTs providing data on the overall efficacy of acupuncture and 12 RCTs providing data on the overall safety of acupuncture. Overall, we did not find strong evidence in support of acupuncture as an efficacious intervention for SUDs, either as an adjunctive or monotherapy. No significant effects were found for relapse, treatment dropout, quantity of substance use, and health-related quality of life. We did identify statistically significant, clinically medium effects in favor of acupuncture (as an adjunctive or monotherapy) versus any comparator for withdrawal/craving at postintervention (SMD −0.57; 95% confidence interval [CI] −0.93 to −0.20; 20 RCTs), frequency of substance use at short-term follow-up (SMD −0.79; CI −1.38 to −0.21; 1 RCT), and functional status (anxiety) at postintervention (SMD −0.74; CI −1.15 to −0.33; 6 RCTs), though these results were based on low or very low quality of evidence due to attrition bias, high heterogeneity, and/or wide confidence intervals. (Note: All CIs reported in this study are at the 95-percent level.) From limited safety data, we did not find strong evidence indicating that acupuncture is associated with any serious adverse events, though a small proportion of participants experienced mild adverse events (e.g., slight bleeding/pain at acupuncture site). A detailed overview of these results is presented in the following sections. Figures 3.2 through 3.7 depict forest plots of acupuncture versus comparators, showing the SMDs and/or ORs with CIs for relevant studies.

### *Relapse*

Ten RCTs (24 percent of RCTs) with 1,175 participants (22 percent of randomized participants) reported relapse data; relapse was measured either as the number of participants who relapsed (as identified by clinical observation or by self-report) or the number of positive toxicology tests. When the data were pooled across the studies, no statistically significant difference between acupuncture (as adjunctive or monotherapy versus any comparator) was observed up to one-month postintervention (SMD −0.12; CI −0.46 to 0.22; $I^2$ 67.3%; see Figure 3.2). There was, however, substantial heterogeneity between the studies. The quality of this body of evidence is very low due to attrition bias, substantial heterogeneity, and wide confidence intervals—limiting confidence that this effect estimate lies close to the true effect of acupuncture on relapse. This effect estimate did not substantially differ at short-term (six-month) follow-up (SMD −0.11; CI −0.63 to 0.40; $I^2$ = 48.8%; 4 RCTs), again based on a very low quality body of evidence.

**Figure 3.2. Acupuncture Versus Any Comparator on Substance Use Relapse**




### *Frequency of Substance Use*

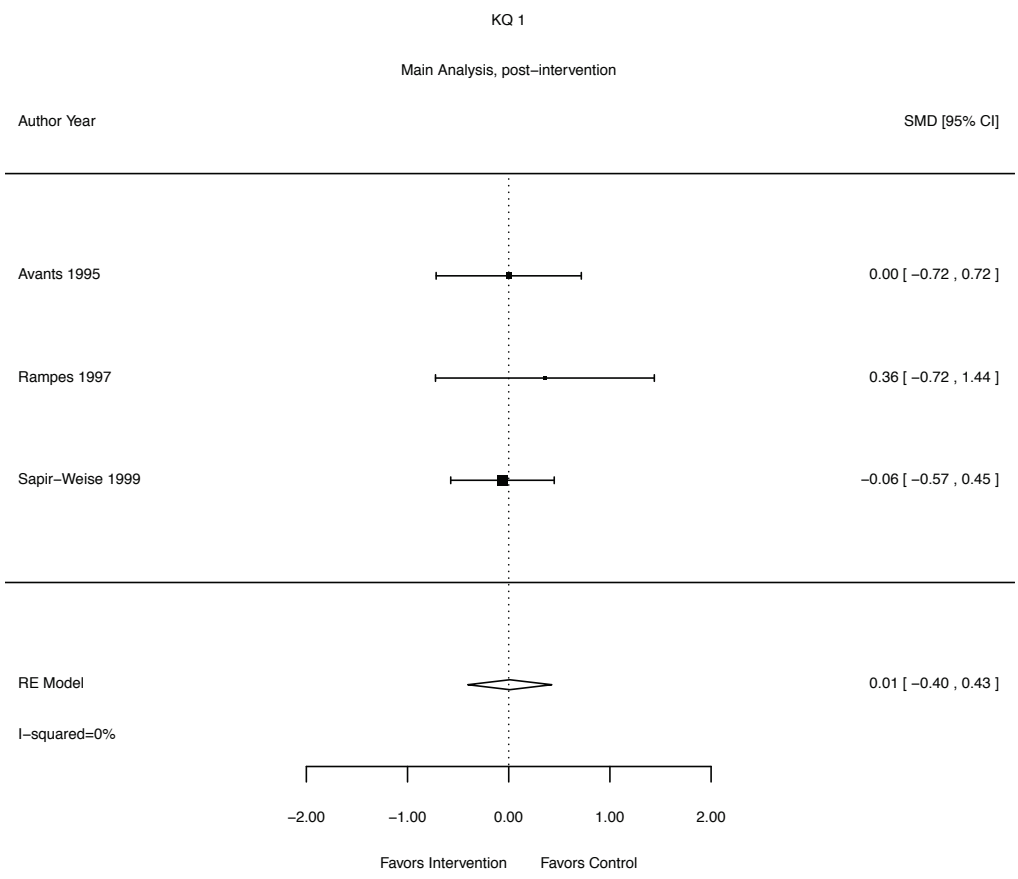
Only two RCTs (5 percent of RCTs) with 120 participants (2 percent of randomized participants) reported data on frequency of substance use, either as the number of days per week or the number of substance use episodes within a given time frame. When data were pooled across the two studies, no significant effect of acupuncture (as adjunctive or monotherapy versus any comparator) was observed up to one-month postintervention (SMD −0.27; CI −2.67 to 2.13; $I^2$ 0%), but this body of evidence is of low quality. There was a medium effect at short-term (six-month) follow-up in favor of acupuncture (as an adjunctive therapy to TAU [drug therapy and psychosocial intervention]) versus sham acupuncture (as an adjunctive therapy to TAU) (SMD

−0.79; CI −1.38 to −0.21; $I^2$ 0%), though this was very low quality evidence based on one RCT (Bullock, Culliton, and Olander, 1989).

### *Quantity of Substance Use*

Three RCTs (7 percent of RCTs) with 154 participants (3 percent of randomized participants) reported data on quantity of substance use, either as breathalyzer alcohol level, self-reported amount of substance use per week, or number of participants consuming at allowable substance use levels (defined as consumption of less than 60 g of alcohol per day). When data were pooled across all the studies, there was no significant effect of acupuncture (as adjunctive or monotherapy versus any comparator) up to 0.5 months postintervention (SMD 0.01; CI −0.40 to 0.43; $I^2$ 0%; 3 RCTs; see Figure 3.3), but the body of evidence is of low quality. This effect estimate did not substantially differ at short-term (3.5-month) follow-up (SMD 0.22; CI −0.34 to 0.79; $I^2$ 68.6%; 1 RCT), and the quality of this body of evidence is very low.

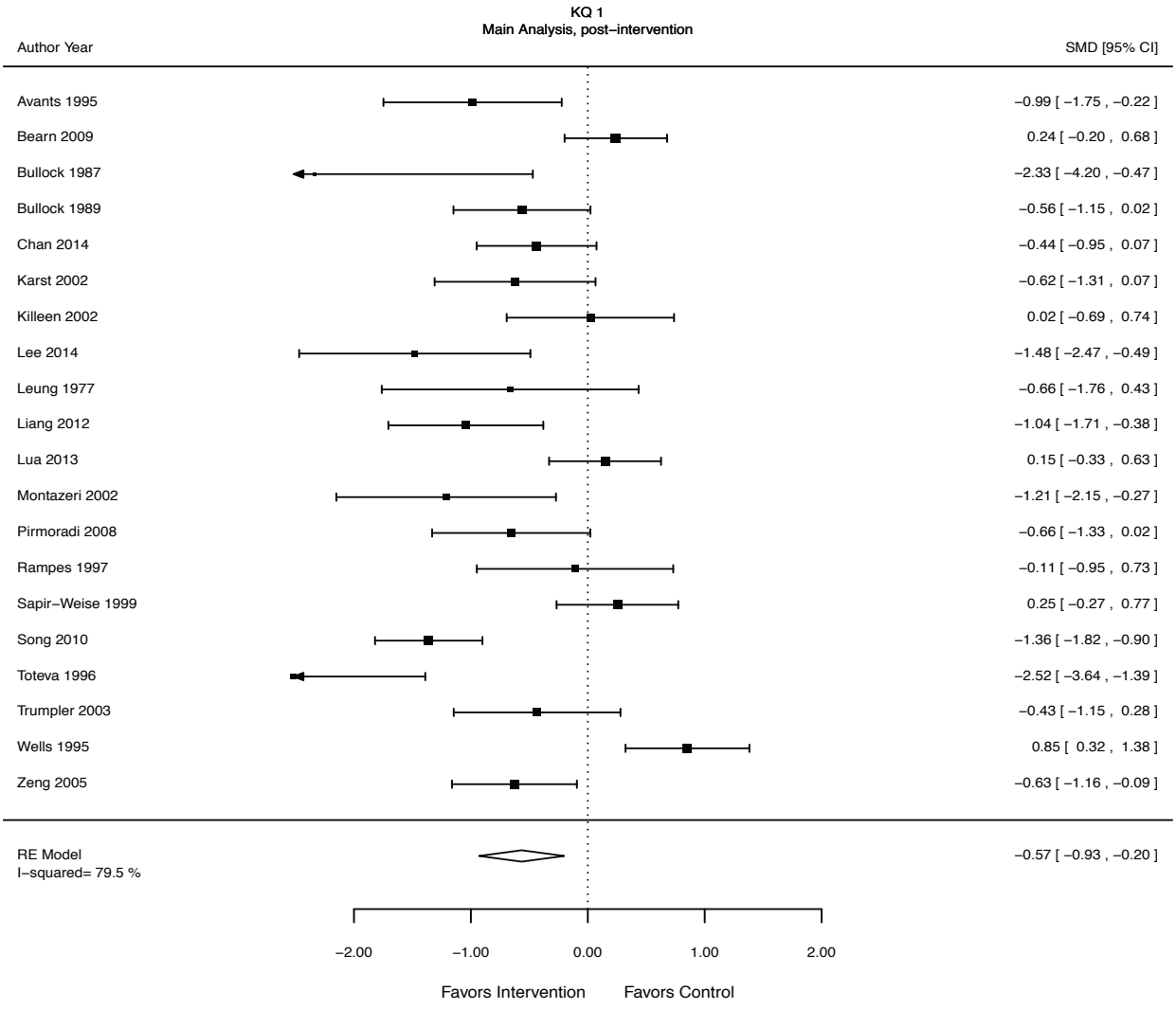
**Figure 3.3. Acupuncture Versus Any Comparator on Quantity of Substance Use**



### *Withdrawal/Craving Symptoms*

Twenty RCTs (49 percent of RCTs) with 1,175 participants (22 percent of randomized participants) reported data on withdrawal or craving symptoms using one of the following measures: the Mainz Alcohol Withdrawal Scale, the Short Opiate Withdrawal Scale, the Clinical Institute Withdrawal Assessment scale, the Cocaine Craving Questionnaire-Now scale, the Penn Alcohol Craving Scale, a visual analog scale, or self-reported symptoms. When data were pooled across all the studies, there was a medium clinical effect in favor of acupuncture (as adjunctive or monotherapy versus any comparator) up to one-month postintervention (SMD −0.57; CI −0.93 to −0.20; $I^2$ 79.5%; 20 RCTs; see Figure 3.4), but there was considerable heterogeneity and suggested evidence of publication bias (see section on Differential Effects by Setting in this chapter), and this body of evidence is of low quality. This effect, however, was no longer statistically significant at short-term (3.5-month) follow-up (SMD −0.32; CI −0.91 to 0.28; $I^2$ 35.4%; 4 RCTs), and the quality of this body of evidence is very low.

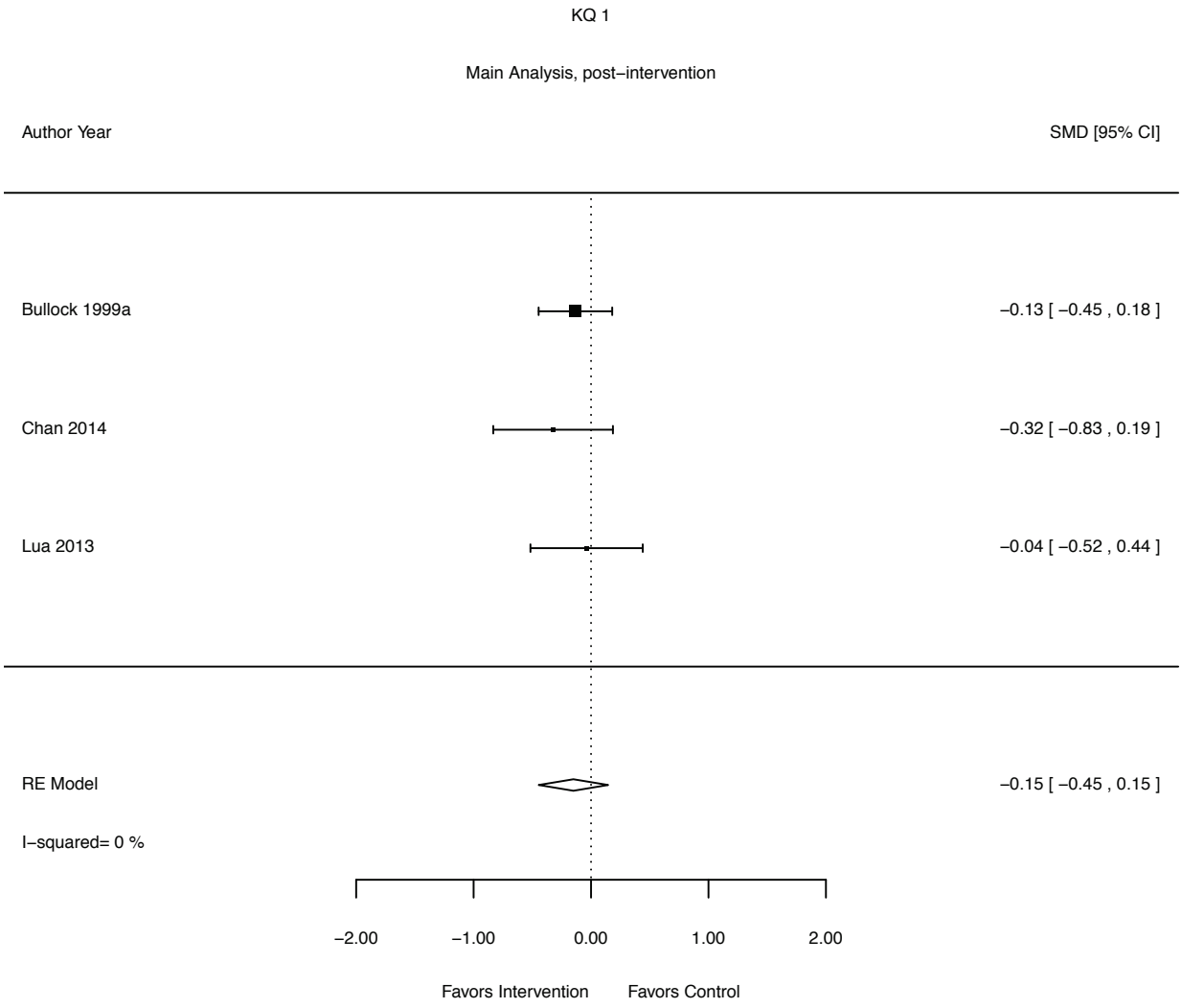
**Figure 3.4. Acupuncture Versus Any Comparator on Withdrawal/Craving Symptoms**




## *Quality of Life*

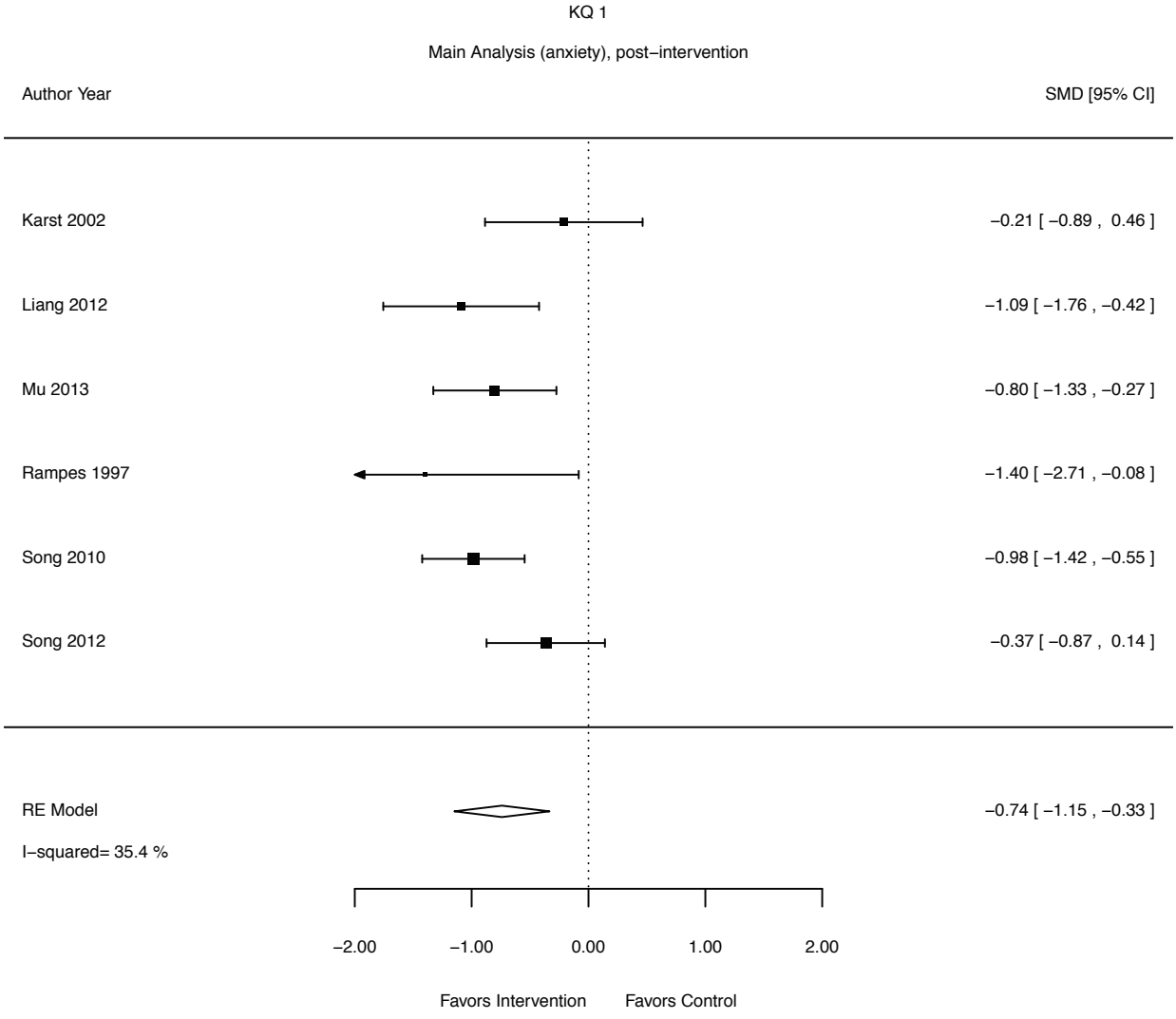
Three RCTs (7 percent of RCTs) with 254 participants (5 percent of randomized participants) reported data on health-related quality of life using one of the following measures: the SF-36 General Health score or an adapted version of the World Health Organization Quality of Life scale. When data were pooled across the studies, there was no statistically significant effect of acupuncture (as adjunctive or monotherapy versus any comparator) at postintervention (SMD −0.15; CI −0.45 to 0.15; $I^2$ 0%; see Figure 3.5), but the body of evidence is of low quality.

**Figure 3.5. Acupuncture Versus Any Comparator on Health-Related Quality of Life**




Six RCTs (15 percent of RCTs) with 329 participants (6 percent of randomized participants) reported data on functional status (anxiety) using one of the following measures: the State-Trait Anxiety Inventory, Clinical Anxiety Scale, Self-Rating Anxiety Scale, or Hamilton Anxiety Scale. When data were pooled across the studies, there was a medium clinical effect in favor of acupuncture (as adjunctive or monotherapy versus any comparator) at postintervention (SMD −0.74; CI −1.15 to −0.33; $I^2$ 35.4%; see Figure 3.6), but the body of evidence is of low quality. Pooled effects, however, were not significant at short-term (3-month) follow-up (SMD −1.15; CI −2.38 to 0.07; $I^2$ 0%; 1 RCT) or when measuring functional status at postintervention in the domains of depression (SMD −0.97; CI −6.74 to 4.81; $I^2$ 73.2%; 2 RCTs), mental state (SMD −0.02; CI −0.48 to 0.43; $I^2$ 0%; 2 RCTs), or social functioning (SMD −0.32; CI −1.49 to 0.84; $I^2$ 0%; 2 RCTs).

**Figure 3.6. Acupuncture Versus Any Comparator on Functional Status (Anxiety)**




### *Recovery Outcomes*

Five RCTs (12 percent of RCTs) reported data on recovery outcomes using one of the following: the Addiction Severity Index, Employment Status score; the Addiction Severity Index, Legal Status score; number of participants incarcerated; or drug court–related outcomes. Due to the clinical heterogeneity of these outcomes, and insufficient reporting in some studies, we could not statistically pool these results and will therefore narratively describe them. The quality of this body of evidence is very low.

- One study found no significant differences for employment problems or legal problems between participants who received auricular acupuncture (as an adjunct to a psychosocial intervention TAU) compared with participants who received sham acupuncture (as an adjunct to TAU) (employment SMD −0.32; CI −0.63 to 0.00; legal problems SMD −0.09;

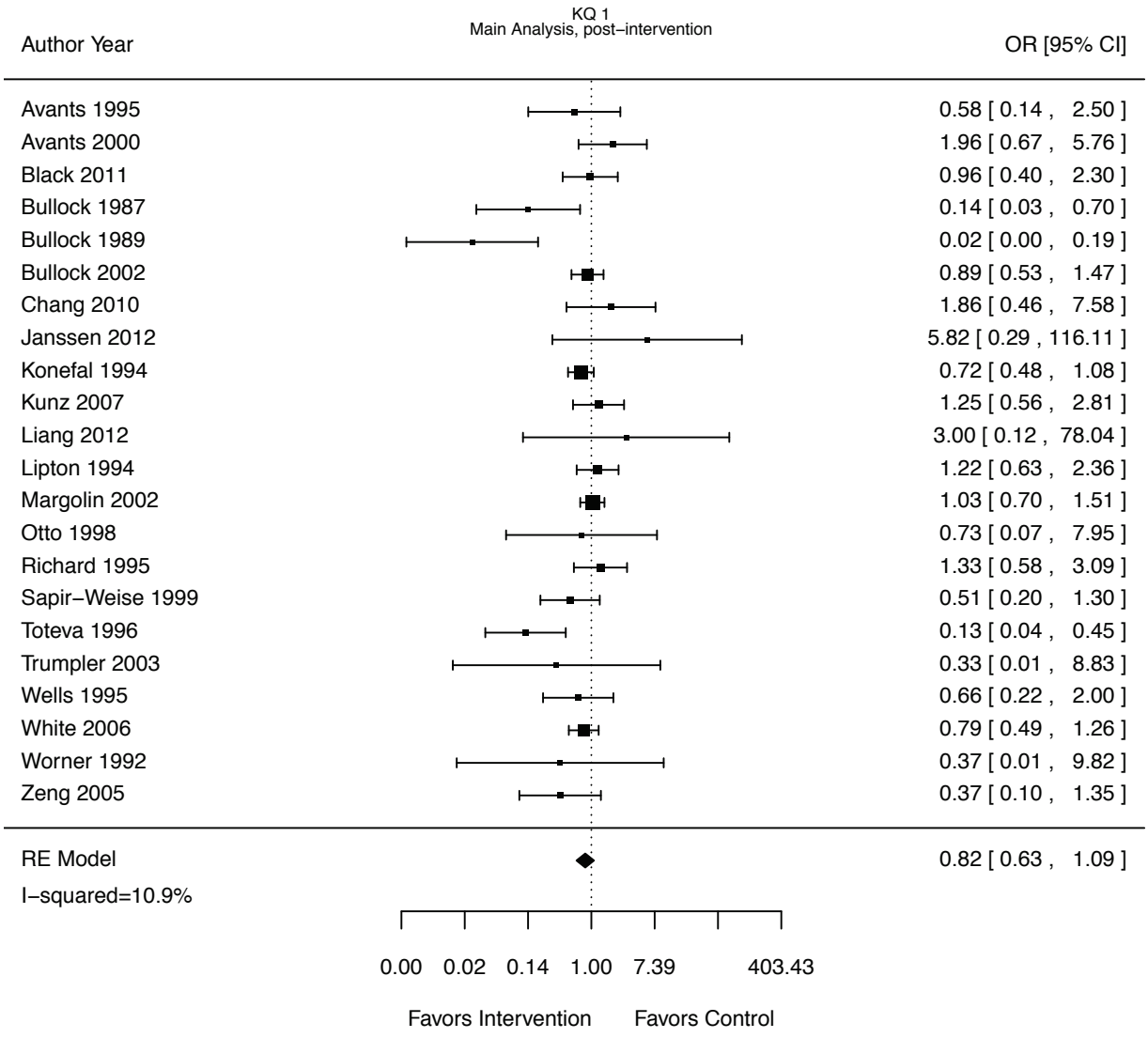
CI −0.40 to 0.23) or compared with participants who received TAU alone (employment SMD −0.20; CI −0.51 to 0.11; legal problems SMD −0.12; CI −0.43 to 0.19) (Bullock, Kiresuk, Pheley, et al., 1999a).

- Another RCT found no significant difference between those who received auricular acupuncture with electrostimulation (as an adjunct to TAU drug therapy) compared with participants who received sham acupuncture involving superficial needle insertion (as an adjunct to TAU) on the number of participants incarcerated (OR 1.00; CI 0.06 to 16.76) (Chan et al., 2014).
- One RCT that compared auricular acupuncture, in combination with drug court psychosocial intervention (TAU), with relaxation therapy (as an adjunct to TAU) found no significant difference between the two groups for re-arrests on new charges (OR 0.96; CI 0.62 to 1.48) (White, Goldkamp, and Robinson, 2006).
- Two other studies reported that some participants dropped out of the study due to incarceration, though they did not mention the intervention conditions of these participants (Lua and Talib, 2013; Rampes et al., 1997).

### *Treatment Dropout*

Twenty-two RCTs (54 percent of RCTs) with 2,768 participants (53 percent of randomized participants) reported data on treatment dropout. This included information on the number of participants receiving or completing treatment, the number of sessions attended, or the number of days in treatment. When dropout data were pooled, there was no statistically significant difference between acupuncture (as adjunctive or monotherapy) versus any comparator at postintervention (OR 0.82; CI 0.63 to 1.09; $I^2$ 10.9%; see Figure 3.7), but this body of evidence was of low quality. This effect estimate did not substantially differ when excluding data on number of sessions attended and restricting analyses only to data on retention/completion of an overall treatment program (in which acupuncture was provided as an adjunctive therapy) (OR 0.87; CI 0.67 to 1.13; $I^2$ 0%; 17 RCTs; see Appendix E, Figure E.1).

**Figure 3.7. Acupuncture Versus Any Comparator on Treatment Dropout**




### *Adverse Events*

We identified 12 RCTs (29 percent of RCTs) with 1,221 participants (23 percent of randomized participants) providing data on the overall safety of acupuncture, reported as local side effects, convulsions, delirium tremens, slight bleeding at the site of acupuncture, treatment withdrawal due to aversion to or actual needle pain, or "adverse events" generally. Only one study reported proactively asking participants about potential side effects, while the other studies passively captured information on adverse events.

Overall, the available evidence on the safety of needle acupuncture for SUDs is limited, as 29 RCTs (71 percent of RCTs) did not report any information on adverse events. Of the safety data reported, we did not find strong evidence indicating that acupuncture is associated with any

serious adverse events. A small proportion of participants experienced mild adverse events, some of which are due to the needle acupuncture (e.g., bleeding at site of insertion, aversion to pain from insertion), whereas others may be due to co-interventions (such as drug therapy) and the fact that acupuncture is typically used in this context for participants with SUDs undergoing detoxification. The results were as follows:

- In the study that proactively asked participants about potential side effects, 38 to 66 percent of participants receiving auricular acupuncture as an adjunct to drug therapy reported dizziness, tingling sensations, nausea, slight fever, light headache, pain, dry mouth, slight bleeding, and drowsiness (Lua and Talib, 2013).
- One study reported no local side effects or development of delirium tremens by any study participant; however, one participant receiving auricular acupuncture as an adjunct to drug therapy experienced self-limiting generalized convulsions of five minutes in duration on the fifth day of withdrawal while she was sleeping, though this was judged to be a withdrawal-related epileptic seizure on clinical grounds (Trumpler et al., 2003).
- Another study reported no adverse events during or after the study period (Chang, Sommers, and Herz, 2010).
- In a recent RCT, two participants receiving auricular acupuncture (with electrostimulation) and one participant receiving sham acupuncture (superficial needle insertion) reported slight bleeding at the site of acupuncture, with an additional participant experiencing mild hand numbness when receiving acupuncture at acupoints on the hand (Chan et al., 2014).
- In another RCT, six participants receiving acupuncture and drug therapy reported negative side effects such as pain and mild bleeding, whereas five participants receiving aroma therapy and drug therapy reported negative side effects such as agitation, sneezing, negative thoughts, or sore throat (Kunz et al., 2007).
- One trial involved three arms, all receiving some form of acupuncture in combination with a psychosocial intervention (TAU): two participants in the auricular acupuncture arm, five participants in the sham acupuncture arm, and one participant in a symptom-based acupuncture arm withdrew from the study due to aversion to needle pain (Bullock, Kiresuck, Sherman, et al., 2002).
- In another RCT, one participant receiving auricular acupuncture along with drug therapy withdrew from the study due to hospitalization, while another in the sham acupuncture arm passed away (Avants, Margolin, Holford, et al., 2000).
- Another RCT also reported withdrawal from the study due to pain from treatment by a participant in a group receiving sham acupuncture as an adjunct to a psychosocial intervention (Rampes et al., 1997).
- One RCT reported that no participants reported definite complaints or side effects caused by acupuncture treatment (Lee et al., 2014).
- Three other studies reported general side effects without specifically indicating how many participants in the different treatment groups experienced them; these included slight bleeding at the site of needle insertion (Rampes et al., 1997; Washburn et al., 1993), nausea or dizziness (Rampes et al., 1997; Washburn et al., 1993), and pain from or fear of needles (Otto, Quinn, and Sung, 1998).

### *Differential Effects by Setting*

To investigate whether results may vary by severity of SUD, we used treatment setting (i.e., inpatient versus outpatient) as a proxy. We had sufficient data to compare the effect of needle acupuncture by treatment setting (i.e., inpatient versus outpatient) for relapse, treatment dropout, and withdrawal/craving symptoms. Indirect comparisons via meta-regressions of the results of analyses by treatment setting yielded no statistically significant differences in effects for relapse ($p = 0.91$), treatment dropout ($p = 0.33$), and withdrawal/craving symptoms ($p = 0.33$).

To investigate whether results may vary by the geographic region in which the study took place, we categorized studies conducted in Asian countries and compared their pooled results with studies conducted in non-Asian countries. We had sufficient data to compare the effect of needle acupuncture by geographic region (i.e., Asian versus non-Asian countries) for treatment dropout, withdrawal/craving symptoms, and functional status (anxiety). Indirect comparisons via meta-regressions of the results of analyses by geographic region yielded no statistically significant differences in effects for treatment dropout ($p = 0.86$), withdrawal/craving symptoms ($p = 0.26$), and functional status (anxiety) ($p = 0.53$).

It is worth noting here again that we included only English-language RCTs indexed in international databases, because certain regions are likely to be proportionally high in publication bias; as a result, we evaluated publication bias for those outcomes with sufficient data. We found no evidence of publication bias for relapse (Egger's test: $p = 0.23$, Begg's test: $p = 0.60$). For withdrawal/craving symptoms, there was suggested evidence of publication bias for the overall analysis of any needle acupuncture versus any comparator (Egger's test: $p = 0.003$, Begg's test: $p = 0.04$; see Appendix E, Figure E.2 for funnel plot). There was also suggested evidence of publication bias for withdrawal/craving symptoms in the subgroup analyses on RCTs focusing specifically on alcohol use (Egger's test: $p = 0.02$, Begg's test: $p = 0.11$), evaluating auricular acupuncture (Egger's test: $p = 0.01$, Begg's test: $p = 0.11$), and using sham acupuncture as a comparator (Egger's test: $p = 0.01$, Begg's test: $p = 0.07$); however, the corresponding pooled treatment effects were not significant in these analyses. There was no suggested evidence of publication bias for the withdrawal/craving symptom analyses showing statistically significant effects in favor of acupuncture (TCM acupuncture: Egger's test: $p = 0.22$, Begg's test: $p = 0.48$; acupuncture as adjunctive therapy: Egger's test: $p = 0.06$, Begg's test: $p = 0.09$). For treatment dropout, there was suggested evidence of publication bias in the analyses on needle acupuncture following the NADA protocol (Egger's test: $p = 0.04$, Begg's test: $p = 0.14$) and on sham acupuncture as comparator (Egger's test: $p = 0.05$, Begg's test: $p = 0.06$); however, the corresponding pooled treatment effects were not significant in these analyses, and there was no suggested evidence of publication bias for the overall analysis of any needle acupuncture intervention versus any comparator on treatment dropout (Egger's test: $p = 0.25$, Begg's test: $p = 0.34$).

## KQ 1a: Does the Effect of Needle Acupuncture Vary by the Substance Targeted (i.e., Alcohol, Opioids, Stimulants, or Cannabis)?

We identified 11 RCTs that reported on alcohol use specifically, ten RCTs that reported on stimulant use, 13 RCTs that reported on opioid use, and one RCT that reported on cannabis use. The quality of individual studies contributing to these analyses was limited by consistently high attrition; several studies also were at high risk of performance bias (due to lack of participant blinding) and selection bias (due to inappropriate random sequence generation and allocation concealment).

We had sufficient data to compare the effect of needle acupuncture by substance targeted via meta-regression for relapse (alcohol, opioids, and stimulants), treatment dropout (alcohol, opioids, and stimulants), withdrawal/craving (alcohol, opioids, and stimulants), and functional status (alcohol and opioids). Indirect comparisons via meta-regressions of the results of analyses by substance targeted yielded no statistically significant differences in effects for relapse, withdrawal/craving, and functional status. For treatment dropout, the results for alcohol use demonstrated effects significantly more in favor of acupuncture compared with the results for stimulant use; however, results for alcohol use were not significantly different from results for opioid use. A detailed overview of results by substance targeted are presented in the following sections.

### *Alcohol*

In the subgroup of studies that reported on alcohol use, there was no statistically significant effect for acupuncture (as an adjunctive or monotherapy) versus any comparator for relapse at postintervention (SMD −0.61; CI −3.94 to 2.72; $I^2$ 9.1%; 2 RCTs) or short-term follow-up (SMD −0.64; CI −1.49 to 0.21; $I^2$ 0; 2 RCTs), and for frequency of substance use at postintervention (SMD −0.40; CI −0.91 to 0.10; 1 RCT), and the body of evidence for these analyses is of low to very low quality. There was a medium effect in favor of auricular acupuncture as an adjunct to TAU (drug therapy and psychosocial intervention), versus sham acupuncture as an adjunct to TAU, on frequency of substance use at six-month follow-up. However, this is based on one RCT (SMD −0.79; CI −1.38 to −0.21), and this body of evidence is of very low quality. There was no statistically significant effect for quantity of alcohol use at postintervention (SMD 0.01; CI −2.04 to 2.07; $I^2$ 0; 2 RCTs) and at short-term follow-up (SMD 0.22; CI −0.34 to 0.79; 1 RCT), withdrawal/craving at postintervention (SMD −0.79; CI −1.58 to 0.00; $I^2$ 75.8%; 8 RCTs) or at short-term follow-up (SMD −0.19; CI −1.18 to 0.80; $I^2$ 33.4%; 3 RCTs), and functional status at postintervention when measured as anxiety (SMD −0.67; CI −8.00 to 6.67; $I^2$ 59.7%; 2 RCTs) or as depression (SMD −0.97; CI −6.74 to 4.81; $I^2$ 73.2%; 2 RCTs), and the body of evidence for these analyses is of low to very low quality. For treatment dropout, there was very low quality evidence of a medium effect in favor of acupuncture (as an adjunctive or monotherapy) versus

any comparator at postintervention, with substantial heterogeneity (OR 0.34; CI 0.12 to 0.99; $I^2$ 71.1%; 8 RCTs).

### *Stimulants*

In the subgroup of studies that reported on stimulant use, there was no statistically significant effect for acupuncture (as an adjunctive or monotherapy) versus any comparator for relapse at postintervention (SMD −0.07; CI −0.57 to 0.44; $I^2$ 75.5; 6 RCTs) or short-term follow-up (SMD −0.07; CI −0.23 to 0.37; 1 RCT), frequency of substance use at postintervention (SMD 0.00; CI −0.72 to 0.72; 1 RCT), quantity of substance use at postintervention (SMD 0.00; CI −0.72 to −0.72; 1 RCT), withdrawal/craving at postintervention (SMD −0.47; CI −6.87 to 5.93; $I^2$ 72.0%; 2 RCTs), health-related quality of life (SMD −0.13; CI −0.45 to 0.18; 1 RCT), and treatment dropout at postintervention (OR 1.12; CI 0.86 to 1.45; $I^2$ 0%; 6 RCTs). The body of evidence for these analyses is of low to very low quality.

### *Opioids*

In the subgroup of studies that reported on opioid use, there was also no statistically significant effect for acupuncture (as an adjunctive or monotherapy) versus any comparator for relapse at postintervention (SMD 0.21; CI −1.85 to 2.27; $I^2$ 0%; 2 RCTs), and the quality of this body of evidence is low. There was no statistically significant effect for acupuncture on withdrawal/craving at postintervention (SMD −0.43; CI −1.00 to 0.14; $I^2$ 86.4%; 9 RCTs), and the quality of this body of evidence is very low. At three-month follow-up, there was a medium clinical effect in favor of auricular acupuncture (with electrostimulation) as an adjunct to psychosocial intervention TAU versus drug therapy as an adjunct to TAU, though this was based on very low quality evidence from one RCT (SMD −0.58; CI −1.05 to −0.12). There was no statistically significant effect for health-related quality of life at postintervention (SMD −0.17; CI −1.98 to 1.64; $I^2$ 0%; 2 RCTs), and the quality of this body of evidence is low. There was also low quality evidence of a large effect in favor of acupuncture (as an adjunctive or monotherapy) versus any comparator for functional status (anxiety) at postintervention (SMD −0.80; CI −1.30 to −0.29; $I^2$ 29.1%; 4 RCTs), though this effect was not significant for functional status measured as mental state (SMD −0.08; CI −0.59 to 0.43; 1 RCT) or social functioning (SMD −0.17; CI −0.68 to 0.33; 1 RCT). There was no statistically significant effect for treatment dropout at postintervention (OR 0.58; CI 0.12 to 2.69; $I^2$ 0%; 3 RCTs), and the quality of this body of evidence is low.

### *Cannabis*

Only one study reported information on cannabis use specifically, indicating no statistically significant difference in relapse to cannabis use as measured by number of positive urine tests (24 percent positive in auricular acupuncture plus psychosocial intervention TAU versus 23 percent positive in frequent urine testing plus TAU; $\chi^2 = 0.03$, $p = 0.87$).

## KQ 1b: Does the Effect of Needle Acupuncture Vary by Type of Acupuncture (e.g., Auricular Acupuncture)?

As mentioned, 32 RCTs provided data on auricular acupuncture (of which 12 RCTs specifically referred to following the NADA protocol for auricular acupuncture), and nine RCTs evaluated some form of TCM acupuncture. Among all RCTs, seven involved electroacupuncture as well. The quality of individual studies contributing to these analyses was limited by consistently high attrition; several studies of TCM acupuncture also were at high risk of performance bias (due to lack of participant blinding).

We had sufficient data to compare the effect of needle acupuncture by use of auricular acupuncture versus TCM acupuncture for relapse, treatment dropout, and withdrawal/craving symptoms. Indirect comparisons via meta-regressions of the results of analyses by type of acupuncture yielded no statistically significant differences in effects for relapse or treatment dropout. For withdrawal/craving symptoms, RCTs evaluating TCM acupuncture had effects significantly more in favor of the acupuncture intervention group compared with RCTs evaluating auricular acupuncture.

We identified four trials providing direct comparisons of different doses of acupuncture (Bullock, Kiresuk, Pheley, et al., 1999b; Konefal, Duncan, and Clemence, 1995; Margolin, Avants, and Arnold, 2005; Bullock, Kiresuck, Sherman, et al., 2002). There was no statistically significant difference of higher doses of acupuncture (either as more auricular points or more sessions) for relapse (SMD −0.11; CI −2.66 to 2.44; $I^2$ 21.1%; 2 RCTs), health-related quality of life (SMD 0.23; CI −0.11 to 0.57; 1 RCT), functional status in the domains of anxiety (SMD 0.38; CI −0.25 to 1.00, 1 RCT) or depression (SMD 0.12; CI −0.50 to 0.74; 1 RCT), or treatment dropout (OR 1.45; CI 0.40 to 5.28; $I^2$ 0%; 2 RCTs).

### *Auricular*

There was no statistically significant effect for auricular acupuncture (as an adjunctive or monotherapy) versus any comparator for relapse at postintervention (SMD −0.11; CI −0.49 to 0.28; $I^2$ 71%; 9 RCTs) and at short-term follow-up (SMD −0.01; CI −0.50 to 0.47; $I^2$ 0%; 3 RCTs) and for frequency of substance use at postintervention (SMD −0.27; CI −2.67 to 2.13; $I^2$ 0%; 2 RCTs); the body of evidence for these analyses is of low to very low quality. There was a medium clinical effect in favor of auricular acupuncture as an adjunct to TAU (drug therapy and psychosocial intervention) versus sham acupuncture (nonspecific points) as an adjunct to TAU for frequency of substance use at short-term follow-up (SMD −0.79; CI −1.38 to −0.21); however, this effect in favor of auricular acupuncture is based on very low quality evidence from one RCT. There was no statistically significant effect of auricular acupuncture on the quantity of substance use at postintervention (SMD 0.01; CI −0.40 to 0.43; $I^2$ 0%; 3 RCTs) and at short-term follow-up (SMD 0.22; CI −0.34 to 0.79; 1 RCT) and for withdrawal/craving at postintervention (SMD −0.29; CI −0.64 to 0.05; $I^2$ 69.7%; 15 RCTs) and at short-term follow-up (SMD −0.32; CI

−0.91 to 0.28; $I^2$ 35.4%; 4 RCTs), and the body of evidence for these analyses is of low to very low quality. There was a large clinical effect in favor of auricular acupuncture (with electrostimulation) as an adjunct to psychosocial intervention TAU versus TAU alone for functional status (anxiety) at postintervention (SMD −1.40; CI −2.71 to −0.08); however, this effect is based on very low quality evidence from one RCT. There was no statistically significant effect of auricular acupuncture on treatment dropout at postintervention (OR 0.88; CI 0.69 to 1.12; $I^2$ 0%; 18 RCTs), and the quality of this body of evidence is low.

### *Auricular Acupuncture Using the NADA Protocol*

There was no statistically significant effect for the subgroup of auricular acupuncture trials specifically referencing the NADA protocol (as an adjunctive or monotherapy) versus any comparator for relapse (SMD −0.22; CI −7.04 to 6.60; $I^2$ 76.3%; 2 RCTs), withdrawal/craving (SMD 0.17; CI −0.07 to 0.41; $I^2$ 0%; 3 RCTs), health-related quality of life (SMD −0.04; CI −0.52 to 0.44; 1 RCT), and treatment dropout (OR 0.99; CI 0.72 to 1.37; $I^2$ 6.5%; 7 RCTs). There was also no statistically significant effect for the subgroup of auricular acupuncture trials that appeared compatible with the NADA protocol (as an adjunctive or monotherapy) versus any comparator for relapse (SMD −0.15; CI −0.60 to 0.30; $I^2$ 70.0%; 8 RCTs), frequency of use (SMD −0.27; CI −2.67 to 2.13; $I^2$ 0%; 2 RCTs), quantity of use (SMD −0.04; CI −0.41 to 0.33; $I^2$ 0%; 2 RCTs), withdrawal/craving (SMD −0.04; CI −0.53 to 0.45; $I^2$ 72.3%; 8 RCTs), health-related quality of life (SMD −0.19; CI −1.23 to 0.85; $I^2$ 0%; 2 RCTs), and treatment dropout (OR 1.06; CI 0.56 to 1.99; $I^2$ 71.2%; 16 RCTs).

### *TCM Acupuncture*

There was no statistically significant effect for TCM acupuncture (as an adjunctive or monotherapy) versus any comparator on relapse at postintervention (SMD −0.31; CI −1.06 to 0.43; 1 RCT) and at short-term follow-up (SMD −0.57; CI −1.36 to 0.22; 1 RCT), and the body of evidence for these analyses is of very low quality. There was a large clinical effect in favor of TCM acupuncture (as an adjunctive or monotherapy) versus any comparator for withdrawal/craving at postintervention (SMD −1.32; CI −2.12 to −0.53; $I^2$ 61.7%; 5 RCTs), though this was based on very low quality of evidence and had substantial heterogeneity. There was no statistically significant effect for functional status (anxiety) at postintervention (SMD −0.73; CI −1.53 to 0.06; $I^2$ 40.3%; 3 RCTs) and for treatment dropout at postintervention (OR 0.29; CI 0.05 to 1.51; $I^2$ 20.7%; 4 RCTs), and the body of evidence for these analyses is of low quality.

### *Electroacupuncture*

There was no statistically significant effect for acupuncture (as an adjunctive or monotherapy) involving electrostimulation versus any comparator for relapse (SMD −0.57; CI −1.36 to 0.22; 1 RCT); quantity of use (SMD 0.36; CI −0.72 to 1.44; 1 RCT);

withdrawal/craving symptoms (SMD −0.73; CI −1.49 to 0.04; $I^2$ 60.9%; 6 RCTs); health-related quality of life (SMD −0.32; CI −0.83 to 0.19; 1 RCT); and functional status measured as anxiety (SMD −0.88; CI −3.50 to 1.74; $I^2$ 0%; 2 RCTs), social functioning (SMD −0.17; CI −0.68 to 0.33; 1 RCT), or mental state (SMD −0.08; CI −0.59 to 0.43; 1 RCT). It is worth noting, however, that the two studies included in the functional status (anxiety) meta-analysis both reported statistically significant effects in favor of acupuncture (Mu et al., 2013: SMD −0.80; CI −1.33 to −0.27; Rampes et al., 1997: SMD −1.40; CI −2.71 to −0.08), with the Hartung-Knapp-Sidik-Jonkman random-effects method yielding a wide confidence interval for the meta-analysis. There was a large clinical effect in favor of TCM acupuncture (with electrostimulation) as an adjunct to TAU drug therapy versus TA alone for functional status measured as depression (SMD −1.41; CI −2.03 to −0.79), though this was based on very low quality of evidence from one RCT. There was no statistically significant effect for acupuncture on treatment dropout (OR 0.21; CI 0.00 to 221.87; $I^2$ 28.6%; 2 RCTs).

## KQ 1c: Does the Effect of needle Acupuncture Differ If Acupuncture Is Offered as an Adjunctive Therapy Rather Than as a Monotherapy?

Thirty-four RCTs provided data on acupuncture as an adjunctive therapy. The other seven RCTs provided data on acupuncture as a monotherapy. Of the 34 adjunctive RCTs, co-interventions involved drug therapy alone for 13 RCTs, psychosocial intervention for ten RCTs, a combination of drug therapy and psychosocial intervention for six RCTs, and one RCT each for drug therapy with a spiritual therapy, TAU with frequent urine testing, generic structured activities, drug court programming, and an undetailed usual care. In addition, 23 of the adjunctive therapy RCTs were two-arm studies in which acupuncture and the comparator were adjunctive therapy to the same intervention, four RCTs were multi-arm studies in which acupuncture and one comparator were adjunctive therapy to the same intervention (Bullock, Kiresuk, Pheley, et al., 1999a; Rampes et al., 1997; Richard et al., 1995; Worner et al., 1992), and 11 RCTs provided a comparator that was a monotherapy (Bullock, Kiresuk, Pheley, et al., 1999a; Janssen et al., 2012; Lua and Talib, 2013; Man and Chuang, 1980; Montazeri, Farahnakian, and Saghaei, 2002; Mu et al., 2013; Rampes et al., 1997; Richard et al., 1995; Song, Hu, et al., 2010; Worner et al., 1992; Zeng et al., 2005). The quality of individual studies contributing to these analyses was limited by consistently high attrition.

Our presentation of results for acupuncture as an adjunctive therapy focuses on findings from meta-analyses of adjunctive therapy versus all comparators. As results may differ depending on whether the comparator is also an adjunctive therapy, we have provided sensitivity analyses pooling those studies evaluating acupuncture as an adjunctive therapy to a comparator that is also an adjunctive therapy separately from those studies with a comparator that is a monotherapy.

We had sufficient data to compare the effect of needle acupuncture as an adjunctive therapy versus needle acupuncture as a monotherapy for relapse, treatment dropout, withdrawal/craving

symptoms, and functional status (anxiety). Indirect comparisons via meta-regressions of adjunctive versus monotherapy yielded no statistically significant differences in effects for relapse, treatment dropout, withdrawal/craving symptoms, and functional status.

### *Adjunctive Therapy Versus All Comparators*

There was no statistically significant effect for acupuncture as an adjunctive therapy versus all comparators for relapse at postintervention (SMD −0.14; CI −0.54 to 0.26; $I^2$ 65.8%; 9 RCTs) or at short-term follow-up (SMD −0.01; CI −0.50 to 0.47; $I^2$ 0%; 3 RCTs), frequency of substance use at postintervention (SMD −0.27; CI −2.67 to 2.13; $I^2$ 0%; 2 RCTs), and quantity of substance use at postintervention (SMD 0.01; CI −0.40 to 0.43; $I^2$ 0%; 3 RCTs) or short-term follow-up (SMD 0.22; CI −0.34 to 0.79; 1 RCT); the body of evidence for these analyses is of low to very low quality. There was a medium clinical effect in favor of acupuncture as an adjunctive therapy versus all comparators for frequency of substance use at short-term follow-up (SMD −0.79; CI −1.38 to −0.21), though this was based on very low quality of evidence from one RCT. There was very low quality evidence of no statistically significant effect for withdrawal/craving symptoms at short-term follow-up (SMD −0.32; CI −0.91 to 0.28; $I^2$ 80.6%; 18 RCTs), though there was a small clinical effect in favor of acupuncture as an adjunctive therapy versus all comparators for withdrawal/craving symptoms at postintervention (SMD −0.43; CI −0.79 to −0.06; $I^2$ 79.7%; 15 RCTs). There was no statistically significant effect for health-related quality of life at postintervention (SMD −0.15; CI −0.45 to 0.15; $I^2$ 0%; 3 RCTs), and the quality of this body of evidence is low. There was low quality evidence for a medium effect in favor of acupuncture as an adjunctive therapy versus all comparators for functional status (anxiety) at postintervention (SMD −0.78; CI −1.42 to −0.15; $I^2$ 32%; 4 RCTs), though this effect was not significant for functional status measured as depression (SMD −0.97; CI −6.74 to 4.81; $I^2$ 73.2%; 2 RCTs), mental state (SMD −0.02; CI −0.48 to 0.43; $I^2$ 0%; 2 RCTs), or social functioning (SMD −0.32; CI −1.49 to 0.84; $I^2$ 0%; 2 RCTs). There was no statistically significant effect for treatment dropout at postintervention (OR 0.86; CI 0.68 to 1.08; $I^2$ 0%; 18 RCTs), and the quality of this body of evidence is low.

When analyzing acupuncture as adjunctive therapy with no comparator to match the acupuncture intervention (e.g., acupuncture plus TAU versus TAU), there was no significant effect for relapse (SMD 0.26; CI −0.85 to 1.38; $I^2$ 51.9%; 3 RCTs), withdrawal/craving symptoms at postintervention (SMD −0.81; CI −2.33 to 0.71; $I^2$ 80.6%; 4 RCTs) or short-term follow-up (SMD −0.33; CI −1.47 to 0.81; 1 RCT), quantity of use (SMD 0.36; CI −0.72 to 1.44; 1 RCT), health-related quality of life (SMD −0.10; CI −0.66 to 0.45; $I^2$ 0%; 2 RCTs), functional status (anxiety) postintervention (SMD −0.88; CI −3.50 to 1.74; $I^2$ 0%; 2 RCTs), and treatment dropout (OR 1.15; CI 0.57 to 2.32; $I^2$ 58.4%; 7 RCTs). It is worth noting, however, that the two studies included in the functional status (anxiety) meta-analysis both reported statistically significant effects in favor of acupuncture (Mu et al., 2013: SMD −0.80; CI −1.33 to −0.27;

Rampes et al., 1997: SMD −1.40; CI −2.71 to −0.08), with the Hartung-Knapp-Sidik-Jonkman random-effects method yielding a wide confidence interval for the meta-analysis.

When analyzing acupuncture as adjunctive therapy with a comparator to match the acupuncture intervention (e.g., acupuncture plus TAU versus relaxation response therapy plus TAU), there was no significant effect for relapse at postintervention (SMD −0.23; CI −0.57 to 0.11; $I^2$ 53.7%; 8 RCTs) or short-term follow-up (SMD −0.01; CI −0.50 to 0.47; $I^2$ 0%; 3 RCTs); quantity of use at postintervention (SMD −0.04; CI −0.41 to 0.33; $I^2$ 0%; 2 RCTs) or at short-term follow-up (SMD 0.22; CI −0.34 to 0.79; 1 RCT); withdrawal/craving symptoms at postintervention (SMD −0.41; CI −0.84 to 0.02; $I^2$ 81.8%; 12 RCTs) or at short-term follow-up (SMD −0.32; CI −0.91 to 0.28; $I^2$ 35.4%; 4 RCTs); health-related quality of life (SMD −0.19; CI −1.23 to 0.85; $I^2$ 0%; 2 RCTs); functional status measured as anxiety (SMD −0.43; CI −1.85 to 0.99; $I^2$ 70.6%; 3 RCTs), mental state (SMD −0.16; CI −0.77 to 0.45; $I^2$ 0%; 2 RCTs), or social functioning (SMD −0.20; CI −0.41 to 0.01; $I^2$ 0%; 2 RCTs); and treatment dropout (OR 0.89; CI 0.70 to 1.14; $I^2$ 0%; 16 RCTs).

### *Monotherapy Versus All Comparators*

There was no statistically significant effect for acupuncture as a monotherapy versus all comparators for relapse at postintervention (SMD −0.06; CI −0.40 to 0.28; 1 RCT) or at short-term follow-up (SMD −0.57; CI −1.36 to 0.22; 1 RCT), withdrawal/craving symptoms at short-term follow-up (SMD −1.17; CI −2.50 to 0.16; $I^2$ 76.4%; 5 RCTs), functional status (anxiety) at postintervention (SMD −0.69; CI −5.27 to 3.88; $I^2$ 65.2%; 2 RCTs), and treatment dropout at postintervention (OR 0.42; CI 0.04 to 4.37; $I^2$ 79%; 4 RCTs). The body of evidence for these analyses is of low to very low quality.

When analyzing TCM acupuncture as monotherapy versus no treatment, there was a large clinical effect in favor of TCM acupuncture as monotherapy versus no treatment for withdrawal/craving symptoms at postintervention (SMD −1.04; CI −1.71 to −0.38), though this is based on very low quality evidence from one RCT. There was no statistically significant effect for treatment dropout (OR 3.00; CI 0.12 to 78.04; 1 RCT).

When analyzing acupuncture (either auricular or TCM) as monotherapy versus active comparators (either sham acupuncture or drug therapy), there was no statistically significant effect for withdrawal/craving at postintervention (SMD −1.26; CI −3.28 to 0.75; $I^2$ 79%; 4 RCTs) or treatment dropout (OR 0.30; CI 0.01 to 8.21; $I^2$ 85.1%; 3 RCTs).

## KQ 1d: Does the Effect of Needle Acupuncture on Substance Use Disorders Depend on the Comparator?

As mentioned, seven RCTs provided data for acupuncture plus TAU versus TAU alone, 19 RCTs for acupuncture versus sham acupuncture, seven RCTs for acupuncture versus a passive comparator, and 16 RCTs for acupuncture versus an active comparator. In addition, four RCTs

provided different doses of acupuncture as comparators. The quality of individual studies contributing to these analyses was limited by consistently high attrition; several studies contributing to acupuncture plus TAU versus TAU analyses and to active comparator analyses also were at high risk of performance bias (due to lack of participant blinding).

We had sufficient data to compare the effect of needle acupuncture by type of comparator for relapse (TAU alone, sham acupuncture, and passive comparator), withdrawal/craving symptoms (TAU alone, sham acupuncture, passive comparator, and active comparator), functional status measured as anxiety (sham acupuncture and passive comparator), and treatment dropout (TAU alone, sham acupuncture, passive comparator, and active comparator). Indirect comparisons via meta-regressions of the results of analyses by type of comparator yielded no statistically significant differences in effects for relapse, withdrawal/craving symptoms, functional status, and treatment dropout.

### *Acupuncture Plus TAU Versus TAU Alone*

There was no statistically significant effect for acupuncture plus TAU versus TAU for relapse at postintervention (SMD 0.26; CI −0.85 to 1.38; $I^2$ 51.9%; 3 RCTs), quantity of substance use (SMD 0.36; CI −0.72 to 1.44; 1 RCT), withdrawal/craving symptoms at postintervention (SMD −0.81; CI −2.33 to 0.71; $I^2$ 80.6%; 4 RCTs) or at short-term follow-up (SMD −0.33; CI −1.47 to 0.81; 1 RCT), health-related quality of life (SMD −0.10; CI −0.66 to 0.45; $I^2$ 0%; 2 RCTs), functional status (anxiety) at postintervention (SMD −0.88; CI −3.50 to 1.74; $I^2$ 0%; 2 RCTs), and treatment dropout (OR 1.15; CI 0.57 to 2.32; $I^2$ 58.4%; 7 RCTs). The body of evidence for these analyses is of low to very low quality. It is worth noting, however, that the two studies included in the meta-analysis that reported on functional status (anxiety) both reported statistically significant effects in favor of acupuncture (Mu et al., 2013: SMD −0.80; CI −1.33 to −0.27; Rampes et al., 1997: SMD −1.40; CI −2.71 to −0.08), with the Hartung-Knapp-Sidik-Jonkman random-effects method yielding a wide confidence interval for the meta-analysis.

### *Sham Acupuncture*

There was no statistically significant effect for acupuncture versus sham acupuncture for relapse at postintervention (SMD −0.07; CI −0.36 to 0.22; $I^2$ 23.8%; 7 RCTs) or at short-term follow-up (SMD −0.24; CI −5.06 to 4.58; $I^2$ 73.2%; 2 RCTs), and the body of evidence for these analyses is of low to very low quality. There was very low quality evidence of a medium clinical effect in favor of auricular acupuncture (as an adjunctive therapy to drug therapy and psychosocial intervention TAU) versus sham acupuncture plus TAU for frequency of use at short-term follow-up (SMD −0.79; CI −1.38 to −0.21), and this very low quality evidence was based on only one RCT. There was no statistically significant effect of acupuncture versus sham acupuncture on frequency of use at postintervention (SMD −0.27; CI −2.67 to 2.13; $I^2$ 0%; 2 RCTs); quantity of use at postintervention (SMD 0.00; CI −0.26 to 0.25; $I^2$ 0%; 3 RCTs) or at short-term follow-up (SMD 0.22; CI −0.34 to 0.79; 1 RCT); withdrawal/craving symptoms at

postintervention (SMD −0.32; CI −0.79 to 0.15; $I^2$ 73.8%; 12 RCTs) or at short-term follow-up (SMD −0.79; CI −1.38 to −0.21; $I^2$ 33.4%; 3 RCTs); health-related quality of life (SMD −0.19; CI −1.23 to 0.85; $I^2$ 0%; 2 RCTs); functional status at postintervention measured as anxiety (SMD −0.09; CI −2.06 to 1.88; $I^2$ 0%; 2 RCTs), mental state (SMD −0.16; CI −0.77 to 0.45; $I^2$ 0%; 2 RCTs), or social functioning (SMD −0.20; CI −0.41 to 0.01; $I^2$ 0%; 2 RCTs); and treatment dropout (OR 0.74; CI 0.41 to 1.34; $I^2$ 55.3%; 11 RCTs). The body of evidence for these analyses is of low to very low quality.

### *Passive Comparator*

There was no statistically significant effect for acupuncture versus a passive comparator for relapse at postintervention (SMD −0.24; CI −5.44 to −4.96; $I^2$ 86.3%; 2 RCTs); it is worth noting, however, that one of studies reported a statistically significant effect in favor of acupuncture (Avants, Margolin, Holford, et al., 2000: SMD −0.68; CI −1.20 to −0.16), with the Hartung-Knapp-Sidik-Jonkman random-effects method yielding a wide confidence interval for the meta-analysis. There was no statistically significant effect for acupuncture versus a passive comparator for relapse at short-term follow-up (SMD −0.19; CI −0.50 to 0.12; 1 RCT), withdrawal/craving symptoms (SMD −1.00; CI −2.16 to 0.16; $I^2$ 56.5%; 3 RCTs), functional status (anxiety) at postintervention (SMD −0.80; CI −1.76 to 0.17; $I^2$ 52.7%; 3 RCTs), and treatment dropout (OR 1.46; CI 0.54 to 3.99; $I^2$ 45.9%; 5 RCTs). The body of evidence for these analyses is of low to very low quality.

### *Active Comparator*

There was no statistically significant effect for acupuncture versus an active comparator for relapse at postintervention (SMD −0.23; CI −0.92 to 0.46; 1 RCT) or at short-term follow-up (SMD −0.15; CI −3.32 to 3.02; $I^2$ 46.2%; 2 RCTs), and for withdrawal/craving symptoms at postintervention (SMD −1.16; CI −3.74 to 1.43; $I^2$ 78%; 3 RCTs); the body of evidence for these analyses is of very low quality. There was a medium clinical effect of auricular acupuncture (with electrostimulation) plus psychosocial intervention TAU versus drug therapy plus TAU for withdrawal/craving at short-term follow-up (SMD −0.58; CI −1.05 to −0.12); however, this was based on very low quality evidence from only one RCT. There was no statistically significant effect for treatment dropout (OR 0.71; CI 0.38 to 1.33; $I^2$ 60.9%; 8 RCTs), and the quality of this body of evidence is very low.

# Chapter Four: Discussion

## Summary of Findings

Overall, the available evidence suggests no consistent effect of acupuncture versus comparator interventions on substance use outcomes, though we observed some positive effects for improving withdrawal/craving symptoms and decreasing anxiety. There were positive results on withdrawal/craving symptoms for acupuncture (as adjunctive or monotherapy versus any comparator) both when TCM acupuncture was evaluated against any comparator and when acupuncture was provided as an adjunctive therapy. The body of evidence underlying these analyses, however, is of low or very low quality due to attrition bias, high heterogeneity, and/or wide confidence intervals. In addition, results for withdrawal/craving were not statistically significant in other subgroup analyses, and the overall analysis has suggested evidence for publication bias. Positive results for anxiety were evident in the KQ 1 analysis, KQ 1a analysis for opioid use, KQ 1b analysis for auricular acupuncture, and KQ 1c analysis for acupuncture as an adjunctive therapy; however, these results also are based on low or very low quality of evidence. Other statistically significant effects were typically based on one trial, with very low confidence in effect estimates. The available evidence suggests that acupuncture is not typically associated with serious adverse events, though adverse events were rarely assessed; some participants may experience slight bleeding/pain at the needle insertion site. See Table 4.1 for a summary of findings and quality of evidence for this review.

Meta-regressions indicated that some results differed by the type of substance targeted (treatment dropout results were statistically significant for alcohol use) and by acupuncture type (pooled analyses of RCTs evaluating TCM acupuncture had effects significantly more in favor of the acupuncture intervention group compared with pooled analyses of RCTs evaluating auricular acupuncture for withdrawal/craving symptoms and treatment dropout). We found no robust evidence to suggest that effects of needle acupuncture differed systematically as an adjunctive therapy or monotherapy, or by the type of comparator. However, these results are limited by the quality of evidence and the limited power to detect statistically significant differences due to the number of studies and the amount of participants within studies.

It is worth noting that acupuncture interventions varied by dosage (e.g., number of sessions and weeks), acupoints (e.g., auricular, auricular following the NADA protocol, TCM points), and co-interventions (e.g., drug therapy, psychosocial intervention), all of which provide sources of clinical heterogeneity. Long-term effects of acupuncture are uncertain, for most outcome data were from postintervention or shortly thereafter, and only eight RCTs provided data after two months. There is also significant attrition in this body of evidence, given that treatments often targeted a hard-to-reach population. Of note, no RCTs focused on active military or veterans.

**Table 4.1. Quality of Evidence and Summary of Findings**

| Outcome[a] | Study Design (number of RCTs and participants) | Findings (direction and magnitude of effect)[b] | Study Limitations (study quality; risk of bias) | Inconsistency | Indirectness | Imprecision | GRADE of Evidence for Outcome |
|---|---|---|---|---|---|---|---|
| KQ 1: Acupuncture versus nonacupuncture for substance use | | | | | | | |
| Substance use relapse (post) | 10 RCTs, 1,175 participants | SMD −0.12 (CI −0.46 to 0.22), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Substance use relapse (short-term) | 4 RCTs, 959 participants | SMD −0.11 (CI −0.63 to 0.40), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Frequency of use (post) | 2 RCTs, 120 participants | SMD −0.27 (CI −2.67 to 2.13), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 2[i] | Very low |
| Frequency of use (short-term) | 1 RCT, 80 participants | SMD −0.79 (CI −1.38 to −0.21), medium effect, acupuncture | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Quantity of use (post) | 3 RCTs, 154 participants | SMD 0.01 (CI −0.40 to 0.43), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Quantity of use (short-term) | 1 RCT, 72 participants | SMD 0.22 (CI −0.34 to 0.79), no significant effect | Downgrade 1[e,f] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 20 RCTs, 1,175 participants | SMD −0.57, (CI −0.93 to −0.20), medium effect, acupuncture | No downgrade | Downgrade 1[g] | Direct | Downgrade 1[i] | Low |
| Withdrawal/craving (short-term) | 4 RCTs, 291 participants | SMD −0.32 (CI −0.91 to 0.28), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Health-related quality of life (post) | 3 RCTs, 254 participants | SMD −0.15 (CI −0.45 to 0.15), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Functional status—anxiety (post) | 6 RCTs, 329 participants | SMD −0.74 (CI −1.15 to −0.33), medium effect, acupuncture | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Functional status—anxiety (short-term) | 1 RCT, 42 participants | SMD −1.15 (CI −2.38 to 0.07), no significant effect | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Recovery—legal problems (post) | 1 RCT, 236 participants | SMD −0.09 (CI −0.40 to 0.23), no significant effect | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Recovery—incarceration (post) | 1 RCT, 60 participants | OR 1.00 (CI 0.06 to 16.76), no significant effect | No downgrade | Downgrade 1[h] | Direct | Downgrade 2[i] | Very low |
| Treatment dropout (post) | 22 RCTs, 2,768 participants | OR 0.82 (CI 0.63 to 1.09), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| KQ 1a: Acupuncture versus any comparator for alcohol | | | | | | | |
| Substance use relapse (post) | 2 RCTs, 169 participants | SMD −0.61 (CI −3.94 to 2.72), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |

| Outcome[a] | Study Design (number of RCTs and participants) | Findings (direction and magnitude of effect)[b] | Study Limitations (study quality; risk of bias) | Inconsistency | Indirectness | Imprecision | GRADE of Evidence for Outcome |
|---|---|---|---|---|---|---|---|
| Substance use relapse (short-term) | 2 RCTs, 198 participants | SMD −0.64 (CI −1.49 to 0.21), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Frequency of use (post) | 1 RCT, 80 participants | SMD −0.40 (CI −0.91 to 0.10), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Frequency of use (short-term) | 1 RCT, 80 participants | See KQ 1 | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Quantity of use (post) | 2 RCTs, 114 participants | SMD 0.01 (CI −2.04 to 2.07), no significant effect | Downgrade 1[c,e,f] | Consistent | Direct | Downgrade 2[i] | Very low |
| Quantity of use (short-term) | 1 RCT, 72 participants | See KQ 1 | Downgrade 1[e,f] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 8 RCTs, 452 participants | SMD −0.79 (CI −1.58 to 0.00), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (short-term) | 3 RCTs, 195 participants | SMD −0.19 (CI −1.18 to 0.80), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Functional status—anxiety (post) | 2 RCTs, 76 participants | SMD −0.67 (CI −8.00 to 6.67), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 2[i] | Very low |
| Treatment dropout (post) | 8 RCTs, 764 participants | OR 0.34 (CI 0.12 to 0.99), medium effect, acupuncture | Downgrade 1[c,d] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| KQ 1a: Acupuncture versus any comparator for stimulants | | | | | | | |
| Substance use relapse (post) | 6 RCTs, 1,080 participants | SMD −0.16 (CI −0.85 to 0.52), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Substance use relapse (short-term) | 1 RCT, 425 participants | SMD −0.07 (CI −0.23 to 0.37), no significant effect | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Frequency of use (post) | 1 RCT, 40 participants | SMD 0.00 (CI −0.72 to 0.72), no significant effect | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Quantity of use (post) | 1 RCT, 40 participants | SMD 0.00 (CI −0.72 to 0.72), no significant effect | Downgrade 1[c,e,f] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 2 RCTs, 70 participants | SMD −0.47 (CI −6.87 to 5.93), no significant effect | No downgrade | Downgrade 1[g] | Direct | Downgrade 2[i] | Very low |
| Health-related quality of life(post) | 1 RCT, 157 participants | SMD −0.13 (CI −0.45 to 0.18), no significant effect | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Treatment dropout (post) | 6 RCTs, 795 participants | OR 1.12 (CI 0.86 to 1.45), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| KQ 1a: Acupuncture versus any comparator for opioids | | | | | | | |
| Substance use relapse (post) | 2 RCTs, 197 participants | SMD 0.21 (CI −1.85 to 2.27), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Withdrawal/craving (post) | 9 RCTs, 657 participants | SMD −0.43 (CI −1.00 to 0.14), no significant effect | Downgrade 1[d] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |

| Outcome[a] | Study Design (number of RCTs and participants) | Findings (direction and magnitude of effect)[b] | Study Limitations (study quality; risk of bias) | Inconsistency | Indirectness | Imprecision | GRADE of Evidence for Outcome |
|---|---|---|---|---|---|---|---|
| Withdrawal/craving (short-term) | 1 RCT, 96 participants | SMD −0.58 (CI −1.05 to −0.12), medium effect, acupuncture | Downgrade 1[d] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Health-related quality of life (post) | 2 RCTs, 157 participants | SMD −0.17 (CI −1.98 to 1.64), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Functional status—anxiety (post) | 4 RCTs, 253 participants | SMD −0.80 (CI −1.30 to −0.29), large effect, acupuncture | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Treatment dropout (post) | 3 RCTs, 171 participants | OR 0.58 (CI 0.12 to 2.69), no significant effect | Downgrade 1[d] | Consistent | Direct | Downgrade 1[i] | Low |
| KQ 1b: Auricular acupuncture versus any comparator | | | | | | | |
| Substance use relapse (post) | 9 RCTs, 1,140 participants | SMD −0.11 (CI −0.49 to 0.28), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Substance use relapse (short-term) | 3 RCTs, 841 participants | SMD −0.01 (CI −0.50 to 0.47), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Frequency of use (post) | 2 RCTs, 120 participants | See KQ 1 | Downgrade 1[c] | Downgrade 2[g] | Direct | Downgrade 1[i] | Very low |
| Frequency of use (short-term) | 1 RCT, 80 participants | See KQ 1 | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Quantity of use (post) | 3 RCTs, 154 participants | See KQ 1 | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Quantity of use (short-term) | 1 RCT, 72 participants | See KQ 1 | Downgrade 1[e,f] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 15 RCTs, 837 participants | SMD −0.29 (CI −0.64 to 0.05), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (short-term) | 4 RCTs, 291 participants | See KQ 1 | No downgrade | Downgrade 1[g] | Direct | Downgrade 1[i] | Low |
| Functional status—anxiety (post) | 1 RCT, 42 participants | SMD −1.40 (CI −2.71 to −0.08), large effect, acupuncture | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Treatment dropout (post) | 18 RCTs, 2,414 participants | OR 0.88 (CI 0.69 to 1.12), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| KQ 1b: TCM acupuncture versus any comparator | | | | | | | |
| Substance use relapse (post) | 1 RCT, 35 participants | SMD −0.31 (CI −1.06 to 0.43), no significant effect | Downgrade 1[d] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Substance use relapse (short-term) | 1 RCT, 118 participants | SMD −0.57 (CI −1.36 to 0.22), no significant effect | Downgrade 1[c,e,f] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 5 RCTs, 338 participants | SMD −1.32 (CI −2.12 to −0.53), large effect, acupuncture | Downgrade 1[d] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |

| Outcome[a] | Study Design (number of RCTs and participants) | Findings (direction and magnitude of effect)[b] | Study Limitations (study quality; risk of bias) | Inconsistency | Indirectness | Imprecision | GRADE of Evidence for Outcome |
|---|---|---|---|---|---|---|---|
| Functional status—anxiety (post) | 3 RCTs, 212 participants | SMD −0.73 (CI −1.53 to 0.06), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Treatment dropout (post) | 4 RCTs, 264 participants | OR 0.29 (0.05 to 1.51), no significant effect | Downgrade 1[d] | Consistent | Direct | Downgrade 1[i] | Low |
| KQ 1c: Acupuncture as an adjunctive therapy versus any comparator | | | | | | | |
| Substance use relapse (post) | 9 RCTs, 1,025 participants | SMD −0.14 (CI −0.54 to 0.26), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Substance use relapse (short-term) | 3 RCTs, 841 participants | See KQ 1b (auricular) | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Frequency of use (post) | 2 RCTs, 120 participants | See KQ 1 | Downgrade 1[c] | Consistent | Direct | Downgrade 2[i] | Very low |
| Frequency of use (short-term) | 1 RCT, 80 participants | See KQ 1 | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Quantity of use (post) | 3 RCTs, 154 participants | See KQ 1 | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Quantity of use (short-term) | 1 RCT, 72 participants | See KQ 1 | Downgrade 1[e,f] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 15 RCTs, 915 participants | SMD −0.43 (CI −0.79 to −0.06), small effect, acupuncture | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (short-term) | 4 RCTs, 291 participants | See KQ 1 | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Health-related quality of life (post) | 3 RCTs, 314 participants | See KQ 1 | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Functional status—anxiety (post) | 4 RCTs, 226 participants | SMD −0.78 (CI −1.42 to −0.15), medium effect, acupuncture | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Treatment dropout (post) | 18 RCTs, 2,315 participants | OR 0.86 (CI 0.68 to 1.08), no significant effect | Downgrade 1[d] | Consistent | Direct | Downgrade 1[i] | Low |
| KQ 1c: Acupuncture as monotherapy versus any comparator | | | | | | | |
| Substance use relapse (post) | 1 RCT, 150 participants | SMD −0.06 (CI −0.40 to 0.28), no significant effect | Downgrade 1[c,e,f] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Substance use relapse (short-term) | 1 RCT, 118 participants | SMD −0.57 (CI −1.36 to 0.22), no significant effect | Downgrade 1[c,e,f] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 5 RCTs, 260 participants | SMD −1.17 (−2.50 to 0.16), no significant effect | No downgrade | Downgrade 1[g] | Direct | Downgrade 1[i] | Low |
| Functional status— | 2 RCTs, | SMD −0.69 (CI −5.27 to | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |

| Outcome[a] | Study Design (number of RCTs and participants) | Findings (direction and magnitude of effect)[b] | Study Limitations (study quality; risk of bias) | Inconsistency | Indirectness | Imprecision | GRADE of Evidence for Outcome |
|---|---|---|---|---|---|---|---|
| anxiety (post) | 103 participants | 3.88), no significant effect | | | | | |
| Treatment dropout (post) | 4 RCTs, 363 participants | OR 0.42 (CI 0.04 to 4.37), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| KQ 1d: Acupuncture + TAU versus TAU | | | | | | | |
| Substance use relapse (post) | 3 RCTs, 289 participants | SMD 0.26 (CI −0.85 to 1.38), no significant effect | Downgrade 1[c,d] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Quantity of use (post) | 1 RCT, 42 participants | SMD 0.36 (CI −0.72 to 1.44), no significant effect | Downgrade 1[c,d] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 4 RCTs, 249 participants | SMD −0.81 (CI −2.33 to 0.71), no significant effect | Downgrade 1[c,d] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (short-term) | 1 RCT, 42 participants | SMD −0.33 (CI −1.47 to 0.81), no significant effect | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Health-related quality of life (post) | 2 RCTs, 254 participants | SMD −0.10 (CI −0.66 to 0.45), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Functional status—anxiety (post) | 2 RCTs, 102 participants | SMD −0.88 (CI −3.50 to 1.74), no significant effect[j] | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Treatment dropout (post) | 7 RCTs, 973 participants | OR 1.25 (CI 0.57 to 2.32), no significant effect | Downgrade 1[d] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| KQ 1d: Acupuncture versus sham acupuncture | | | | | | | |
| Substance use relapse (post) | 7 RCTs, 619 participants | SMD −0.07 (CI −0.36 to 0.22), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Substance use relapse (short-term) | 2 RCTs, 505 participants | SMD −0.24 (CI −5.06 to 4.58), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Frequency of use (post) | 2 RCTs, 120 participants | See KQ 1 | Downgrade 1[c] | Consistent | Direct | Downgrade 2[i] | Very low |
| Frequency of use (short-term) | 1 RCT, 80 participants | SMD −3.74 (CI −4.67 to −2.81), large effect, acupuncture | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Quantity of use (post) | 3 RCTs, 155 participants | SMD 0.00 (CI −0.26 to 0.25), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Quantity of use (short-term) | 1 RCT, 72 participants | See KQ 1 | Downgrade 1[e,f] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 12 RCTs, 592 participants | SMD −0.32 (CI −0.79 to 0.15), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (short-term) | 3 RCTs, 195 participants | SMD −0.79 (CI −1.38 to −0.21), medium effect, acupuncture | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Health-related quality of life (post) | 2 RCTs, 218 participants | SMD −0.19 (CI −1.23 to 0.85), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |

| Outcome[a] | Study Design (number of RCTs and participants) | Findings (direction and magnitude of effect)[b] | Study Limitations (study quality; risk of bias) | Inconsistency | Indirectness | Imprecision | GRADE of Evidence for Outcome |
|---|---|---|---|---|---|---|---|
| Functional status—anxiety (post) | 2 RCTs, 77 participants | SMD −0.09 (CI −2.06 to 1.88), no significant effect | Downgrade 1[c] | Consistent | Direct | Downgrade 1[i] | Low |
| Treatment dropout (post) | 11 RCTs, 1,336 participants | OR 0.74 (CI 0.41 to 1.34), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| KQ 1d: Acupuncture versus passive comparator | | | | | | | |
| Substance use relapse (post) | 2 RCT, 480 participants | SMD −0.24 (CI −5.44 to 4.96), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Substance use relapse (short-term) | 1 RCT, 417 participants | SMD −0.19 (CI −0.50 to 0.12), no significant effect | Downgrade 1[c] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 3 RCTs, 183 participants | SMD −1.00 (CI −2.16 to 0.16), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Functional status—anxiety (post) | 3 RCTs, 193 participants | SMD −0.80 (CI −1.76 to 0.17), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Treatment dropout (post) | 5 RCTs, 630 participants | OR 1.46 (CI 0.54 to 3.99), no significant effect | No downgrade | Downgrade 1[g] | Direct | Downgrade 1[i] | Low |
| KQ 1d: Acupuncture versus active comparator | | | | | | | |
| Substance use relapse (post) | 1 RCTs, 40 participants | SMD −0.23 (CI −0.92 to 0.46), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Substance use relapse (short-term) | 2 RCTs, 454 participants | SMD −0.15 (CI −3.32 to 3.02), no significant effect | Downgrade 1[d] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (post) | 3 RCTs, 246 participants | SMD −1.16 (CI −3.74 to 1.43), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |
| Withdrawal/craving (short-term) | 1 RCT, 96 participants | See KQ 1a (opioids) | Downgrade 1[d] | Downgrade 1[h] | Direct | Downgrade 1[i] | Very low |
| Treatment dropout (post) | 8 RCTs, 1,136 participants | OR 0.71 (CI 0.38 to 1.33), no significant effect | Downgrade 1[c] | Downgrade 1[g] | Direct | Downgrade 1[i] | Very low |

[a] Postintervention is 0–2 months following the end of the intervention, and short-term follow-up is 3–12 months following the end of the intervention.
[b] SMDs less than 0 and ORs less than 1 favor acupuncture. Indices for effect size: SMD 0.2 or OR 0.60 for a small clinical effect; SMD 0.5 or OR 0.29 for a medium clinical effect; and SMD 0.8 or OR 0.15 for a large clinical effect.
[c] High attrition bias.
[d] Performance bias (participant blinding).
[e] Random sequence generation.
[f] Allocation concealment.
[g] Inconsistent due to substantial heterogeneity.
[h] Cannot judge consistency as there was only one RCT.
[i] Wide confidence interval spanning effect sizes with different clinical conclusions.
[j] This was a pooled result of two studies, in which each study individually was statistically significant in favor of acupuncture, though the pooled result using the Hartung-Knapp-Sidik-Jonkman random-effects method was not statistically significant.

## Other Reviews in This Area

The results of this review are comparable to the conclusions of previous meta-analyses that evaluate acupuncture for alcohol dependence (Cho and Whang, 2009) and cocaine dependence (Gates, Smith, and Foxcroft, 2006; Mills et al., 2005). These reviews concluded that there were equivocal results between acupuncture and comparator interventions for substance use outcomes and treatment dropout. Moreover, much like the current review, these reviews indicated that most included studies were hampered by poor methodological quality and loss-to-follow-up, weakening the conclusions that can be drawn from this body of evidence.

Another review on acupuncture combined with opioid receptor agonists found a clinically large and statistically significant effect in favor of acupuncture as an adjunctive therapy for withdrawal symptoms (Liu et al., 2009). The current review also indicates statistically significant effects in favor of acupuncture for withdrawal/craving symptoms at postintervention generally (KQ 1), at short-term follow-up for opiate use specifically (KQ 1a), at postintervention for TCM acupuncture (KQ 1b), at postintervention for adjunctive therapy (KQ 1c), and at short-term follow-up against active comparators (KQ 1d). However, our conclusions differ from the other review for various reasons:

- We generally found medium effects, whereas the other review found quite large effects.
- We conducted a formal assessment of the quality of evidence, which indicated a low or very low quality of evidence and thus lessened our confidence in the effect estimates found.
- Liu et al. (2009)'s review included mostly Chinese-language studies that were excluded from this review.
- Liu et al. (2009) reported positive effects only at days 1, 7, 9, and 10 of treatment, with no positive effects at other days of treatment or at any points postintervention. Our review focused on postintervention and short-term follow-up. The other review also did not find effects for relapse in follow-up periods of up to six months and noted the poor quality of this body of literature—similar to the results of our review.

## Strengths and Limitations

This review has several strengths: an *a priori* research design, duplicate study selection and data abstraction of study information, a comprehensive search of electronic databases, inclusion of gray literature (e.g., dissertations or graduate theses), and risk-of-bias assessments and comprehensive assessments for strength of evidence used to formulate review conclusions. However, some limitations are worth noting. First, we focused only on needle acupuncture, whereas related interventions (e.g., acupressure, laser acupuncture) may yield different effects. Second, we did not contact trial authors to obtain missing data or to identify other potential studies not identified by the search strategy; we did not search some databases specific to complementary and alternative medicine (e.g., Acubriefs, Acudoc2 RCT) that may yield

acupuncture studies not found in major medical databases such as PubMed (Cogo et al., 2011). Third, some meta-analyses in this review pool results from only two RCTs or provide data from only one RCT that has not been replicated. Significant heterogeneity also existed for several outcomes: Given the broad diversity of interventions and the broad area of substance use research, important sources of heterogeneity likely include type of substance targeted by acupuncture treatment, population characteristics, inpatient versus outpatient settings, and methods of outcome measure. Lastly, we also did not consider response expectancies (i.e., participant expectations that acupuncture will have positive effects) in our analyses, though this information was not reported in this body of evidence. In addition to limitations of this review, it is also important to note that the aforementioned attrition biases throughout this literature also limited confidence in findings.

## Implications for Future Research and Practice

Similar to previous reviews in this area, we conclude that the generally poor methodological quality of the body of evidence prevents any strong conclusions about needle acupuncture for SUDs. The available evidence did not yield consistent effects for substance use outcomes. There was evidence of the effectiveness of needle acupuncture on some psychosocial outcomes (namely, withdrawal/craving and anxiety), though the body of evidence for these results is of low to very low quality. This review is consistent with previous reviews' conclusions that more well-designed, rigorous, and large RCTs are needed in order to develop an evidence base that can more decisively provide estimates of the effectiveness of acupuncture for SUDs. As no included study focused on active military or veteran populations, future RCTs incorporating military-related eligibility criteria could provide more-applicable evidence to decisionmakers in military and veteran health systems. Researchers should also consider the potential effect of participant expectancies about acupuncture on intervention outcomes (Mao et al., 2007). In addition, future RCTs should be reported in compliance with the Standards for Reporting Interventions in Controlled Trials of Acupuncture (MacPherson et al., 2002). Researchers, policymakers, funders, and practitioners may wish to convene in order to decide the priorities (if any) for future research on needle acupuncture for SUDs.

# Appendix A: Search Strategy

## Medline on Ovid

**Time Period Covered:**
1948-12/31/2014

**Language:**
English

**Search Strategy:**

1. (trigger point or dry needling or scalp acupuncture or auricular acupuncture or electroacupuncture or electroacupuncture or body acupuncture).af.
2. limit 1 to english language
3. acupuncture.af.
4. acupuncture.af.
5. limit 4 to english language
6. substance-related disorders.sh.
7. limit 6 to english language
8. ((drug or substance$) adj2 (misuse or abuse$ or addict$)).mp.
9. limit 8 to english language
10. (abstinent$ or abstain$).mp.
11. limit 10 to english language
12. withdraw$.mp.
13. limit 12 to english language
14. ((drug$ or polydrug$ or substance$ or alcohol$ or tranquil$ or chemical$ or narcotic$ or opiate$ or street drug$ or solvent$ or inhalant$ or psychotropic$ or intoxica$) and (abus$ or use$ or misus$ or usin$ or utiliz$ or utilis$ or depend$ or addict$ or illegal$ or illicit$ or habit$ or withdraw$ or behavi$ or abstinence$ or abstain$ or rehab$ or intoxica$ or non-prescri$)).mp.
15. limit 14 to english language
16. (dual$ adj diagnos$).mp. or substance-abuse/ or drug-dependence/ or alcohol-abuse/ or alcoholism/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
17. limit 16 to english language
18. 7 or 9 or 11 or 13 or 15 or 17
19. 2 or 5
20. 18 and 19

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## PubMed

**Time Period Covered:**
~1946-12/31/2014

**Language:**
English

**Search Strategy #1:**
acupuncture OR "Acupuncture Therapy"[Mesh] OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*)
AND
drug OR drugs OR substance* OR alcohol* OR tranquilizer* OR tranquiliser* OR chemical OR polydrug* OR narcotic* OR opiate* OR opioid* OR psychotropic* OR intoxic* OR non-prescri*
AND
misuse or abus* or addict* OR illegal OR illicit OR habit* OR withdraw* OR abstinen* OR abstain* OR rehabilitat*

OR

acupuncture OR "Acupuncture Therapy"[Mesh] OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*)
AND
"Substance-Related Disorders"[Mesh] OR cannabis OR marijuana OR marihuana OR cocaine OR heroin OR methamphetamin* OR street drug* OR substance abus* OR substance misus* OR drug abus* OR addict* OR drinking behavior[mh] OR (chemical AND dependen*)

**Search Strategy #2:**
acupuncture OR "Acupuncture Therapy"[Mesh] OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*)
AND
"Substance-Related Disorders"[Mesh] OR cannabis OR marijuana OR marihuana OR cocaine OR heroin OR methamphetamin* OR street drug* OR substance abus* OR substance misus* OR drug abus* OR addict* OR drinking behavior[mh] OR (chemical AND dependen*)
AND
random* OR randomized controlled trial[pt] OR randomized controlled trials OR rct* OR blind* OR double-blind* OR single-blind*

**Search Strategy #3:**
(acupuncture OR "Acupuncture Therapy"[Mesh] OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*))

AND
Methadone

==========

## PsycINFO

**Time Period Covered:**
~1800-11/14/2014

**Language:**
English

**Search Strategy:**
acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*)
AND
cannabis or marijuana or marihuana or cocaine or heroin or methamphetamin* or methadone OR street drug* or substance abus* or substance misus* or drug abus* or addict* or (chemical and dependen*)

OR

acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*)
AND
drug or drugs or substance* or alcohol* or tranquilizer* or tranquiliser* or chemical or polydrug* or narcotic* or opiate* or opioid* or psychotropic* or intoxic* or non-prescri*
AND
misuse or abus* or addict* or illegal or illicit or habit* or withdraw* or abstinen* or abstain* or rehab*

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## CINAHL (Cumulative Index to Nursing and Allied Health Literature)

**Time Period Covered:**
~1/1/1956-11/18/2014

**Language:**
English

**Search Strategy:**
acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*)
AND

drug or drugs or substance* or alcohol* or tranquilizer* or tranquiliser* or chemical or polydrug* or narcotic* or opiate* or opioid* or psychotropic* or intoxic* or non-prescri*
AND
misuse or abus* or addict* or illegal or illicit or habit* or withdraw* or abstinen* or abstain* or rehab*

Search modes - Find all search terms

OR

acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*)
AND
cannabis or marijuana or marihuana or cocaine or heroin or methamphetamin* or methadone OR street drug* or substance abus* or substance misus* or drug abus* or addict* or (chemical and dependen*)

Search modes - Find all search terms

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## AMED (Allied and Complementary Medicine Database)

**Time Period Covered:**
~1/1/1980-11/14/2014

**Language:**
English

**Search Strategy:**
acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*)
AND
(cannabis or marijuana or marihuana or cocaine or heroin or methamphetamin* or street drug* or substance abus* or substance misus* or drug abus* or addict* or (chemical and dependen*)).af.

OR

(acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*)).af.

AND
(drug or drugs or substance* or alcohol* or tranquilizer* or tranquiliser* or chemical or polydrug* or narcotic* or opiate* or opioid* or psychotropic* or intoxic* or non-prescri*)
AND

(misuse or abus* or addict* or illegal or illicit or habit* or withdraw* or abstinen* or abstain* or rehab* or methadone* or substance-related disorder*).af.

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## Cochrane Central Register of Controlled Trials (CENTRAL)

**Time Period Covered:**
~1/1/1970-11/18/2014

**Language:**
English

**Search Strategy:**
acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*):ti,ab,kw
AND
cannabis or marijuana or marihuana or cocaine or heroin or methamphetamin* or methadone or street drug* or substance abus* or substance misus* or drug abus* or addict* or (chemical and dependen*):ti,ab,kw

OR

acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*):ti,ab,kw
AND
drug or drugs or substance* or alcohol* or tranquilizer* or tranquiliser* or chemical or polydrug* or narcotic* or opiate* or opioid* or psychotropic* or intoxic* or non-prescri*:ti,ab,kw
AND
misuse or abus* or addict* or illegal or illicit or habit* or withdraw* or abstinen* or abstain* or rehab*:ti,ab,kw

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## MANTIS (Manual, Alternative, and Natural Therapy Index System)

**Time Period Covered:**
~1/1/1900-11/18/2014

**Language:**
English

**Search Strategy:**
acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*)
AND
(cannabis or marijuana or marihuana or cocaine or heroin or methamphetamin* or street drug* or substance abus* or substance misus* or drug abus* or addict* or (chemical and dependen*)).af.

OR

acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or ("chinese medicine" and needl*)
AND
drug or drugs or substance* or alcohol* or tranquilizer* or tranquiliser* or chemical or polydrug* or narcotic* or opiate* or opioid* or psychotropic* or intoxic* or non-prescri*
AND
(misuse or abus* or addict* or illegal or illicit or habit* or withdraw* or abstinen* or abstain* or rehab*).af.

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## Embase

**Time Period Covered:**
1/1/1980-12/31/2014

**Language:**
English

**Search Strategy:**
'acupuncture'/de OR acupuncture OR 'electroacupuncture'/de OR electroacupuncture OR 'electro acupuncture' OR (acupoint AND stimulat*) OR (meridian AND needl*) OR 'auricular acupuncture' OR ('chinese medicine'/de OR 'chinese medicine') AND needl*))
AND
'substance abuse' OR ('drug'/exp OR drug AND ('dependence'/exp OR dependence)) OR 'alcoholism'/exp OR alcoholism OR 'cannabis'/de OR cannabis OR 'marijuana'/de OR marijuana OR 'marihuana'/de OR marihuana OR 'cocaine'/de OR cocaine OR 'heroin'/de OR heroin OR methamphetamin* OR 'methadone'/de OR methadone OR (street AND drug*) OR (substance AND abus*) OR (substance AND misus*) OR (('drug'/de OR drug) AND abus*) OR addict* OR (chemical AND dependen*)
AND
Humans/lim

The Embase search was further qualified by EndNote filtering on "random*" or "RCT*"

After importing all results into endnote, duplicates and irrelevant material (e.g., animal studies) were removed.

# Appendix B: Evidence Table of Included Studies

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Avants, Margolin, Chang, et al., 1995<br><br>**References:** Avants 1994; Avants, Margolin, Chang, et al., 1995<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Estimate an effect size for the difference between auricular acupuncture and sham acupuncture<br><br>**Quality rating:** Poor<br><br>ITT analysis not used for outcomes besides relapse | **Number of patients:** 40 (20 acupuncture, 20 sham acupuncture)<br><br>**Baseline substance use:** Mean daily methadone dose of 72.6 mg; used opiates for an average of 14 years; used an average of 1.7 g of cocaine for 2.3 days per week; used cocaine regularly for an average of 13.0 years; 47.5% used cocaine intravenously, 37.5% by smoking, and 15% intranasally<br><br>**Comorbid psychological/behavioral health conditions:** 45% were positive for human immunodeficiency virus (HIV); 25% were taking HIV medication; 50% had a DSM-III-R Axis II diagnosis of Antisocial Personality Disorder<br><br>**Age (Years):** 35.2 (SD 7.4)<br><br>**Gender:** 55% male<br><br>**Inclusion criteria:** Enrolled in inner-city methadone program, maintained on a stable dose of methadone<br><br>**Exclusion criteria:** Had an outer-ear infection, were actively psychotic or suicidal | **Content of acupuncture intervention:** Daily acupuncture bilaterally in three auricular (lung, Shen Men, sympathetic) sites plus one in each hand (LI-4). Auricular needles inserted to a depth of 2 mm, and into LI 4 to a depth of approximately 10 mm. Needles were 0.20 mm wide and 15 mm long. Trained acupuncturist with 16+ years of experience. Treatments administered in groups after subjects received their daily methadone dose.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 5 times a week for 6 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Maintained on a stable dose of methadone<br><br>**Comparator:** Sham acupuncture within 2–3 mm of the four active sites<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** Insufficient power (post hoc analysis)<br><br>**Follow-up:** Postintervention | **Relapse:** Average number of cocaine positive screens throughout treatment, versus sham acupuncture: SMD −0.15, CI −0.77 to 0.47<br><br>**Frequency of substance use:** Average number of days cocaine used per week at postintervention, versus sham acupuncture: SMD 0.00, CI −0.72 to 0.72<br><br>**Quantity of substance use:** Average number of grams of cocaine used per week at postintervention, versus sham acupuncture: SMD 0.00, CI −0.72 to 0.72<br><br>**Withdrawal/craving symptoms:** Self-reported cocaine craving at postintervention, versus sham acupuncture: SMD −0.99, CI −1.75 to −0.22<br><br>**Treatment dropout:** Number of participants who completed treatment, versus sham acupuncture: OR 0.58, CI 0.14 to 2.50 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Avants, Margolin, Holford, et al., 2000<br><br>**References:** Avants, Margolin, Holford, et al., 2000; Margolin, Kleber, et al., 2002<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Evaluate the effectiveness of auricular acupuncture for the treatment of cocaine addiction<br><br>**Quality rating:** Good<br><br>Reliable measurement, clearly described interventions, ITT analysis used | **Number of patients:** 82 (28 acupuncture, 27 sham acupuncture, 27 passive comparator)<br><br>**Baseline substance use:** All patients had reached a stable dose of methadone of 78 mg per day<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** 37 (SD 6)<br><br>**Gender:** 57% male<br><br>**Inclusion criteria:** Cocaine- and opioid-dependent patients enrolled in an inner-city methadone maintenance treatment (MMT) program and were referred to the study because of unremitting cocaine use; age of at least 18 years; maintenance on a stable dose of methadone; meeting criteria for cocaine dependence according to the Structured Clinical Interview for DSM-IV; evidence of recent cocaine use<br><br>**Exclusion criteria:** Dependence on any substance other than opiates, cocaine, or nicotine; current treatment for cocaine dependence; current use of a psychotropic medication (unless maintained on a regimen for at least 90 days); current acupuncture treatment or use of acupuncture in the previous 30 days; active suicidal or psychotic status | **Content of acupuncture intervention:** Needles were inserted into the auricles bilaterally at four NADA-specified zones (liver, lung, Shen Men, and sympathetic). Needles were inserted to a depth of between 1 and 3 mm. Needles were 0.20 mm wide and 15 mm long, stainless steel, and disposable. Treatment was delivered after receipt of daily methadone dose. Treatments were delivered in groups of up to six patients. Professional acupuncturist had more than 10 years' experience as an acupuncturist and was certified to provide the NADA protocol.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 5 times a week for 8 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Maintained on a stable dose of methadone<br><br>**Comparator:** (1) Sham acupuncture (zones not commonly used for the treatment of any disorder); (2) passive comparator (videos depicting relaxation strategies, relaxing music)<br><br>**Primary endpoint:** Relapse at postintervention<br><br>**Power calculation:** *A priori* power calculation; targeted sample size achieved<br><br>**Follow-up:** Postintervention | **Relapse:** Average number of consecutive urine-free samples at postintervention, versus sham acupuncture: SMD −0.70, CI −1.25 to −0.16; versus passive comparator: SMD −0.68, CI −1.20 to −0.16<br><br>**Treatment dropout:** Number of participants who completed treatment, versus sham acupuncture: OR 1.96, CI 0.67 to 5.76; versus passive comparator: OR 5.08, CI 1.50 to 17.24<br><br>**Adverse events:** One participant (3.7%) in the sham acupuncture group died during the study. One participant (3.6%) in the acupuncture group withdrew from treatment due to hospitalization. |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Bearn, et al., 2009<br><br>**References:** Bearn, et al., 2009<br><br>**Country:** United Kingdom<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Investigate whether adjunctive treatment with auricular acupuncture enhances the effectiveness of oral methadone detoxification treatment by reducing the severity of opiate withdrawal symptoms and craving<br><br>**Quality rating:** Poor<br><br>ITT analysis not used | **Number of patients:** 82 (48 acupuncture, 34 sham acupuncture)<br><br>**Baseline substance use:** Heroin: 73% acupuncture participants, 77% sham; Codeine: 19% acupuncture, 9% sham; Cocaine powder: 6% acupuncture, 9% sham; Crack cocaine: 56% acupuncture, 67% sham; Amphetamines: 2% acupuncture, 3% sham; Cannabis: 29% acupuncture, 38% sham; Mean methadone stabilizing dose (mg): 53.1 (22.4) acupuncture, 55.2 (14.7) sham<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** Acupuncture: 36.2 (SD 7.0); sham acupuncture: 35.7 (SD 6.2)<br><br>**Gender:** Acupuncture: 73% male; sham acupuncture: 79% male<br><br>**Inclusion criteria:** Met DSM-IV criteria for opiate dependence; referred for inpatient detoxification<br><br>**Exclusion criteria:** Major physical or psychiatric comorbidity; concurrent treatment with antidepressant or neuroleptic medication; pregnancy; ear infection; or topical eczema | **Content of acupuncture intervention:** Needles were inserted into the auricles bilaterally at four NADA-specified zones (liver, lung, Shen Men, and sympathetic). Needles were inserted to a depth of between 1 and 3 mm. Needles were 0.20 mm wide and 15 mm long, stainless steel, and disposable. Treatment was delivered after receipt of daily methadone dose. Treatments were delivered in groups of up to six patients. Professional acupuncturist had more than 10 years' experience as an acupuncturist and was certified to provide the NADA protocol.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30- to 40-minute sessions, 5 times a week for 2 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Standard detoxification treatment with methadone. Structured care program during and after detoxification treatment, consisting of group and individual sessions, targeted at relapse prevention<br><br>**Comparator:** Sham acupuncture (five metal clips)<br><br>**Primary endpoint:** Withdrawal at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Severity of withdrawal symptoms using Short Opiate Withdrawal Scale at postintervention, versus sham acupuncture: SMD 0.24, CI −0.20 to 0.68 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Black, et al., 2011<br><br>**References:** Black, et al., 2011<br><br>**Country:** Canada<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Test the hypothesis that the NADA protocol reduces anxiety associated with withdrawal from psychoactive drugs<br><br>**Quality rating:** Poor<br><br>ITT analysis not used | **Number of patients:** 140 (45 acupuncture, 54 sham acupuncture, 41 passive comparator)<br><br>**Baseline substance use:** Nicotine (31.7%), alcohol (28.7%), cocaine (16.8%), and cannabis (10.9%) were the most commonly reported primary presenting problem<br><br>**Comorbid psychological/behavioral health conditions:** 38% at risk for anxiety<br><br>**Age (Years):** 41.2 (SD 12)<br><br>**Gender:** 51% male<br><br>**Inclusion criteria:** Being at least 18 years of age; self-reported primary presenting problem of alcohol, cocaine, nicotine, cannabis, opioids, benzodiazepines, or amphetamines; not having received acupuncture treatment within the past 3 months; not currently receiving treatment for an anxiety disorder; has no history of coagulation or platelet disorders; is not taking medications that may promote bleeding<br><br>**Exclusion criteria:** None reported | **Content of acupuncture intervention:** Auricular acupuncture with needles inserted into auricles bilaterally at the five NADA protocol specified points (kidney, liver, lung, Shen Men, and sympathetic). Needles were inserted to a depth of 1–3 mm. Needles were 0.22 mm wide and 13 mm long. Treatments were delivered in groups.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 3<br><br>**Dosage:** 45-minute sessions, 1–2 times a week for 2 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Usual standard of care offered by the service area within which they were registered<br><br>**Comparator:** (1) Sham acupuncture (insertion points not described previously for the treatment of addiction or other conditions); (2) passive comparator (relax in dark room with soothing music)<br><br>**Primary endpoint:** Anxiety at postintervention<br><br>**Power calculation:** *A priori* power calculation; targeted sample size achieved<br><br>**Follow-up:** Postintervention | **Treatment dropout:** Number of participants who received allocated treatment, versus sham acupuncture: OR 0.96, CI 0.40 to 2.30; versus passive comparator: OR 1.26, CI 0.48 to 3.29 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Bullock, Umen, et al., 1987<br><br>**References:** Bullock, Umen, et al., 1987<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Evaluate acupuncture for chronic alcoholics<br><br>**Quality rating:** Poor<br><br>High attrition rates, ITT analysis not used | **Number of patients:** 54 (27 acupuncture, 27 sham acupuncture)<br><br>**Baseline substance use:** 98.1% indicated alcohol as their single drug of abuse; less than 15% reported significant use of other drugs (e.g., tranquilizers, sedatives, or marijuana); 68.5% drank daily; 31.5% identified as binge drinkers. Mean years of alcohol abuse were 21 for acupuncture participants and 18 for sham acupuncture.<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** 42<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** Male chronic alcoholics; between the ages of 25 and 65; documentation of at least 20 admissions to detox center, or at least five admissions in the most recent calendar year; previous treatment failure (e.g., refusal to enter treatment, unsuccessful therapy, failed commitment to treatment); no identifiable support person/group(s); no full-time employment for at least 6 months<br><br>**Exclusion criteria:** Taking prescribed steroids or other mood-altering drugs | **Content of acupuncture intervention:** Acupuncture treatments with three ear points (lung, Shen Men, and either liver, kidney, or occiput) specific for chemical dependency, and two wrist points (L.I. 4 Hoku and S.J. 5 Weigaun). Delivered by an experienced acupuncturist. Acupuncture treatments were administered without manual or electrostimulation.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 2–5 times a week for 11 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** None reported<br><br>**Comparator:** Sham acupuncture (ear points not specific for chemical dependency)<br><br>**Primary endpoint:** Treatment dropout at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Number of participants who reported neutral to no need for alcohol at treatment completion at postintervention, versus sham acupuncture: SMD −2.33, CI −4.20 to −0.47<br><br>**Treatment dropout:** Number of participants who completed the final phase of treatment, versus sham acupuncture: OR 0.14, CI 0.03 to 0.70 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Bullock, Culliton, and Olander, 1989<br><br>**References:** Bullock, Culliton, and Olander, 1989<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Assess effectiveness of acupuncture for alcohol use at 6-month follow-up<br><br>**Quality rating:** Poor<br><br>High attrition rates, ITT analysis not used | **Number of patients:** 80 (40 acupuncture; 40 sham acupuncture)<br><br>**Baseline substance use:** 100% reported alcohol as primary drug of abuse; 30% reported past episodic use of other drugs (e.g., sedatives, opioids, stimulants, tranquillizers, cocaine); 40% began abusing alcohol by age 15. Mean years of alcohol abuse was 23 for acupuncture and 21 for sham.<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** 42<br><br>**Gender:** 94% male<br><br>**Inclusion criteria:** Age over 18 years; ten or more total admissions to detoxification center or five admissions in the most recent calendar year; previous inpatient or outpatient treatment failure (e.g., patient left the program); no full-time employment (according to history) for at least the previous six months<br><br>**Exclusion criteria:** Previously received acupuncture therapy; pregnant | **Content of acupuncture intervention:** Acupuncture bilaterally at three ear points regarded as specific for chemical dependency (lung, Shen Men, sympathetic) and a single specific hand point for anxiety (LI 4 Hoku). Acupuncture delivered in a group setting by two experienced acupuncturists. Needles inserted to depth of about 0–5 mm. Acupuncture treatments administered without manual or electrostimulation.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30-minute sessions, 2–5 times a week for 8 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Medications to ease functional complaints and control early signs of alcohol withdrawal. Nursing staff present at all times, rounds made daily by internal medicine resident. Individual counseling and group therapy not provided. All participants attended Alcoholics Anonymous meetings twice a week.<br><br>**Comparator:** Sham acupuncture (ear points not specific for chemical dependency)<br><br>**Primary endpoint:** None reported<br><br>**Power calculation:** *A priori* power calculation; targeted sample size achieved<br><br>**Follow-up:** 6 months | **Relapse:** Number of participants self-reporting abstinence at one-month follow-up, versus sham acupuncture: SMD −0.84, CI −1.49 to −0.19; and at six-month follow-up, versus sham acupuncture: SMD −0.70, CI −1.43 to 0.02<br><br>**Frequency of substance use:** Average number of drinking episodes at one-month postintervention, versus sham acupuncture: SMD −0.40, CI −0.91 to 0.10; and at six-month follow-up, versus sham acupuncture: SMD −0.79, CI −1.38 to −0.21<br><br>**Withdrawal/craving symptoms:** Number of participants with indifferent to no need for alcohol at one-month postintervention, versus sham acupuncture: SMD −0.56, CI −1.15 to 0.02; and at three-month follow-up, versus sham acupuncture: SMD −0.60, CI −1.20 to 0.00<br><br>**Treatment dropout:** Number of participants who completed treatment, versus sham acupuncture: OR 0.02, CI 0.00 to 0.19 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Bullock, Kiresuk, Pheley, et al., 1999a<br><br>**References:** Bullock, Kiresuk, Pheley, et al., 1999<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Examine acupuncture as adjunctive therapy for the treatment of cocaine abuse<br><br>**Quality rating:** Fair<br><br>ITT analysis used, insufficient information provided to judge baseline equivalence or use outcomes in meta-analysis | **Number of patients:** 236 (numbers randomized to each group not reported)<br><br>**Baseline substance use:** Cocaine abuse by all participants<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** 30.2 (SD 6.0)<br><br>**Gender:** 70% male<br><br>**Inclusion criteria:** Receiving treatment for cocaine dependence; free of illicit substances at the time of admission to the detox program, as determined by specially trained intake coordinators; used cocaine at least two times per week for the month preceding study enrollment; were age 18 or above; were not actively psychotic or suffering neurological, physical, or other mental illness that would impair the ability to comprehend the consent form; were willing to participate in a treatment program involving acupuncture; and were not receiving antipsychotic, antidepressant, sedative, stimulant, or other mood-altering medications<br><br>**Exclusion criteria:** None reported | **Content of acupuncture intervention:** Acupuncture at three ear points considered to be specific for substance abuse. Acupuncture treatments delivered in group settings by nationally board-certified acupuncturists. Treatments were administered without manual or electrical stimulation.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 3–5 times a week for 8 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Conventional multicomponent psychosocial programming<br><br>**Comparator:** (1) Sham acupuncture (nonspecific ear points); (2) TAU (conventional multicomponent psychosocial programming)<br><br>**Primary endpoint:** None reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Relapse:** Percentage of participants with positive urine analysis at postintervention, versus sham acupuncture: SMD 0.08, CI −0.29 to 0.44; versus TAU: SMD 0.54, CI 0.18 to 0.90<br><br>**Health-related quality of life:** SF-36 General Health score at postintervention, versus sham acupuncture: SMD −0.14, CI −0.45 to 0.17; versus TAU: SMD −0.13, CI −0.45 to 0.18<br><br>**Functional status:** Addiction Severity Index: Psychiatric Status score at postintervention, versus sham acupuncture: SMD −0.19, CI −0.50 to 0.13; versus TAU: SMD 0.00, CI −0.31 to 0.31. Addiction Severity Index: Family Social Status score at postintervention, versus sham acupuncture: SMD −0.21, CI −0.52 to 0.10; versus TAU: SMD −0.38, CI −0.69 to −0.06.<br><br>**Recovery outcomes:** Addiction Severity Index: Employment Status score at postintervention, versus sham acupuncture: SMD −0.32, CI −0.63 to 0.00; versus TAU: SMD −0.20, CI −0.51 to 0.11. Addiction Severity Index: Legal Status score at postintervention, versus sham acupuncture: SMD −0.09, CI −0.40 to 0.23; versus TAU: SMD −0.12, CI −0.43 to 0.19. |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Bullock, Kiresuk, Pheley, et al., 1999b<br><br>**References:** Bullock, Kiresuk, Pheley, et al., 1999<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Determine the number of acupuncture sessions required to produce an effect<br><br>**Quality rating:** Fair<br><br>High attrition with ITT analysis used, insufficient information to assess baseline differences and outcomes for meta-analysis | **Number of patients:** 202 (numbers randomized to each group not reported)<br><br>**Baseline substance use:** Not reported<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** 30.2<br><br>**Gender:** 70% male<br><br>**Inclusion criteria:** Entering treatment for cocaine dependence; used cocaine at least two times per week for the month preceding study enrollment; were age 18 or above; were not actively psychotic or suffering neurological, physical, or other mental illness that would impair the ability to comprehend the consent form; were willing to participate in a treatment program involving acupuncture; were not receiving antipsychotic, antidepressant, sedative, stimulant, or other mood-altering medications<br><br>**Exclusion criteria:** None reported | **Content of acupuncture intervention:** Five ear points considered to be specific for substance abuse and one wrist point. Treatments were delivered in groups of up to 15 patients.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 3–4 times a week for 8 weeks (28 sessions total)<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Conventional psychosocial programming<br><br>**Comparator:** (1) 16 sessions of the acupuncture protocol; (2) 8 sessions of the acupuncture protocol<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Health-related quality of life:** SF-36 General Health score at postintervention, versus 16 sessions: SMD 0.23, CI −0.11 to 0.57; versus 8 sessions: SMD 0.41, CI 0.07 to 0.75<br><br>**Functional status:** Addiction Severity Index: Psychiatric Status score at postintervention, versus 16 sessions: SMD −0.23, CI −0.56 to 0.11; versus 8 sessions: SMD −0.13, CI −0.47 to 0.20. Addiction Severity Index: Family Social Status score, versus 16 sessions: SMD −0.22, CI −0.55 to 0.12; versus 8 sessions: SMD 0.06, CI −0.28 to 0.39. |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Bullock, Kiresuck, Sherman, et al., 2002<br><br>**References:** Bullock, Kiresuck, Sherman, et al., 2002<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Delineate the role of acupuncture in the treatment of alcoholism<br><br>**Quality rating:** Fair<br><br>Comparable groups with high retention rates, ITT analysis used, reliable measurement, several outcomes not reported sufficiently for meta-analysis | **Number of patients:** 503 (132 acupuncture; 133 sham acupuncture; 134 TAU; 104 symptom-based acupuncture)<br><br>**Baseline substance use:** All participants had spent time in a controlled environment, primarily other chemical dependency programs, during the 30 days prior to intake. The average length of stay was 5.7 days (median 4 days).<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** 38 (SD 10)<br><br>**Gender:** 50% male<br><br>**Inclusion criteria:** Patients in a residential inpatient program; between ages 18 and 66<br><br>**Exclusion criteria:** None reported | **Content of acupuncture intervention:** Acupuncture at four ear points (liver, lung, Shen Men, and sympathetic) specific for chemical dependency. Acupuncture treatment delivered in a group setting by seven highly trained and experienced acupuncturists. Treatments were administered without manual stimulation.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 40-minute sessions, 6 times a week for 3 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** The ‘‘Minnesota Model’’ of treatment emphasizing abstinence-based programming, with individually-tailored services<br><br>**Comparator:** (1) Sham acupuncture (nonspecific ear points); (2) TAU (Minnesota Model); (3) symptom-based acupuncture (tailored to daily presentation of symptoms)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 12 months | **Treatment dropout:** Number of participants who completed treatment, versus sham acupuncture: OR 0.89, CI 0.53 to 1.47; versus TAU: OR 2.29, CI 1.29 to 4.06<br><br>**Adverse events:** Two participants (1.5%) in the acupuncture group, five participants (3.8%) in the sham acupuncture group, and one participant (1.0%) in the symptom-based acupuncture group withdrew from treatment due to aversion to needle pain |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Chan et al., 2014<br><br>**References:** Chan et al., 2014<br><br>**Country:** Taiwan<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Examine the effectiveness of acupuncture for heroin addicts on methadone maintenance<br><br>**Quality rating:** Good<br><br>97% follow-up, reliable measurement, clearly described interventions, ITT analysis used | **Number of patients:** 60 (30 acupuncture, 30 sham acupuncture)<br><br>**Baseline substance use:** Heroin and amphetamine abuse histories averaged 7.05 and 5.08 years, respectively. The daily consumption of methadone was 53.01 mg.<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** 36.2<br><br>**Gender:** 82% male<br><br>**Inclusion criteria:** Over 20 years old; fulfilled DSM-IV criteria for opiate dependence; had been receiving MMT for more than 1 month<br><br>**Exclusion criteria:** Received any antidepressant or neuroleptic medication; received any acupuncture treatment during the previous 30 days; developed severe adverse effects or had a history of events relating to acupuncture treatment; any serious physical illness; a significant risk of suicide; an infection close to the site of the selected acupoints; were pregnant or were planning pregnancy; had bleeding disorders or were taking anticoagulant drugs; were HIV positive | **Content of acupuncture intervention:** Auricular acupuncture (Shen Men) and body electroacupuncture (Hegu and Zusanli acupoints). Auricular acupuncture used conventional auricular stud needles consisting of a vertical needle and a horizontal circular piece of metal. Electrical stimulation was done via a portable electroacupuncture machine. Acupuncture treatment was delivered in a group setting by the same qualified acupuncturist with 10 years of clinical experience with acupuncture treatment.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 20-minute sessions, 2 times a week for 4 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Methadone maintenance, with methadone dosage adjusted by an independent psychiatrist<br><br>**Comparator:** Sham acupuncture (superficial needling at same acupoints as acupuncture group)<br><br>**Primary endpoint:** Health-related quality of life at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Health-related quality of life:** SF-36 General Health score at postintervention, versus sham acupuncture: SMD −0.32, CI −0.83 to 0.19<br><br>**Withdrawal/craving symptoms:** 100 mm visual analog scale (VAS) at postintervention, versus sham acupuncture: SMD −0.44, CI −0.95 to 0.07<br><br>**Functional status:** SF-36 General Mental Health score at postintervention, versus sham acupuncture: SMD −0.08, CI −0.59 to 0.43. SF-36 Social Functioning score at postintervention, versus sham acupuncture: SMD −0.17, CI −0.68 to 0.33.<br><br>**Recovery outcomes:** Number of participants incarcerated at postintervention, versus sham acupuncture: OR 1.00, CI 0.06 to 16.76<br><br>**Adverse events:** Two participants (6.7%) in the acupuncture group and one participant (3.3%) in the sham acupuncture group experienced slight bleeding at the site of acupuncture. One participant (3.3%) in the acupuncture group experienced mild hand numbness. |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Chang, Sommers, and Herz, 2010<br><br>**References:** Chang, Sommers, and Herz, 2010; Chang and Sommers, 2014<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Investigate the effect of using acupuncture to treat veterans who are recovering from SUDs<br><br>**Quality rating:** Good<br><br>Comparable groups, reliable measurements, ITT analysis used | **Number of patients:** 67 (23 acupuncture, 23 relaxation response, 21 TAU)<br><br>**Baseline substance use:** 72% indicated that alcohol was their substance of choice<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** Acupuncture: 46.6 (SD 8.3); relaxation response: 49.5 (SD 6.5); TAU: 49.5 (SD 6.1)<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** Veterans' self-report of having a substance abuse/dependence problem of any type of substance; remaining in the domiciliary for at least 10 weeks after study entry in order to complete the study<br><br>**Exclusion criteria:** Schizophrenia or psychotic diagnosis; a bleeding disorder (hemophilia or thrombocytopenia); an allergy to metals (needles) | **Content of acupuncture intervention:** Acupuncture using NADA protocol for five acupuncture points located in the ear (kidney, liver, lung, Shen Men, and sympathetic). Acupuncture treatment delivered in a group setting by experienced acupuncturists required to have a valid and current license from the Committee on Acupuncture of the Massachusetts Board of Registration in Medicine and to be certified by the Department of Veterans Affairs Medical Center in Bedford.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 2 times a week for 10 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Time-limited sober-living residential treatment with a full spectrum of clinical and vocational services, including 12-step and relapse prevention programs<br><br>**Comparator:** (1) Active comparator (relaxation response group with 10 weekly 45-minute groups led by the study clinical psychologist to learn five techniques for eliciting relaxation response); (2) TAU<br><br>**Primary endpoint:** Withdrawal/craving at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Treatment dropout:** Number of participants who completed treatment, versus TAU: OR 1.86, CI 0.46 to 7.58; versus active comparator: OR 0.68, CI 0.20 to 2.31<br><br>**Adverse events:** There were no adverse events reported during or after the study period |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Janssen et al., 2012<br><br>**References:** Janssen et al., 2012<br><br>**Country:** Canada<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Test the ability of maternal acupuncture treatment among mothers who use illicit drugs to reduce the frequency and severity of withdrawal symptoms among their newborns<br><br>**Quality rating:** Good<br><br>More than 80% follow-up, reliable measurement, interventions clearly described, ITT analysis used | **Number of patients:** 89 (50 acupuncture, 39 drug therapy)<br><br>**Baseline substance use:** Participants used various combinations of the following substances on admission to hospital: cigarettes, alcohol, heroin, other opioids, cocaine, crack, cannabis, crystal meth, benzodiazepine, ecstasy, antidepressants<br><br>**Comorbid psychological/behavioral health conditions:** 54% no diagnosis; 18% depression; 12% bipolar; 2% anxiety disorder; 10% psychosis; 1% borderline personality<br><br>**Age (Years):** Acupuncture: 28.2 (SD 5.6); drug therapy: 29 (SD 5.9)<br><br>**Gender:** 0% male<br><br>**Inclusion criteria:** Chemically dependent women living in Vancouver and surrounding suburbs admitted to the Chemical Dependency Unit at BC Women's Hospital<br><br>**Exclusion criteria:** Inability to read or write English; having a pacemaker or other electrical implant; having a bleeding disorder or a condition putting someone at particular risk for infection (e.g., damaged heart valves, diabetes requiring insulin, immunosuppressive drug therapy or open wounds) | **Content of acupuncture intervention:** Acupuncture using NADA protocol in five ear points (kidney, liver, lung, Shen Men, and sympathetic)<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 7 times a week (duration not reported)<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Methadone maintenance program or support to withdraw from methadone and other illicit drugs. Access to a variety of "healing" activities, such as yoga, gardening, therapeutic touch, peer support groups, arts and crafts, group walks, and massage therapy. Sessions with alcohol and drug support counselors are available.<br><br>**Comparator:** Drug therapy (see co-intervention)<br><br>**Primary endpoint:** Number of days of treatment of the newborn with morphine (follow-up not reported)<br><br>**Power calculation:** Insufficient power (post hoc analysis)<br><br>**Follow-up:** Postintervention | **Treatment dropout:** Number of participants who received allocated intervention, versus TAU: OR 5.82, CI 0.29 to 116.11 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Karst et al., 2002<br><br>**References:** Karst et al., 2002<br><br>**Country:** Germany<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Evaluate the efficacy of acupuncture in the treatment of alcohol withdrawal symptoms<br><br>**Quality rating:** Good<br><br>80% follow-up, valid/reliable measurement, clear interventions, ITT analysis used | **Number of patients:** 34 (17 acupuncture, 17 sham acupuncture)<br><br>**Baseline substance use:** Alcohol consumption (g per day): 279 for acupuncture, 311 for sham; Alcohol consumption (years): 11.9 for acupuncture, 12.1 for sham acupuncture<br><br>**Comorbid psychological/behavioral health conditions:** Depression (Beck Depression Inventory): 14.6 for acupuncture, 20.5 for sham acupuncture; anxiety (State-Trait Anxiety Inventory): 50.1 for acupuncture, 50.2 for sham acupuncture<br><br>**Age (Years):** 43.3 (SD 9.0)<br><br>**Gender:** 88% male<br><br>**Inclusion criteria:** alcoholics admitted to the detoxification unit of a medical school; alcohol addiction according to ICD-10 criteria; age over 18 years<br><br>**Exclusion criteria:** Severe hepatic or hematological complications; addiction to other drugs than alcohol; major psychiatric disorder; previously received acupuncture; anticoagulation; pregnancy | **Content of acupuncture intervention:** Needles were inserted bilaterally at auricular acupoints (kidney, liver, lung, Shen Men, and sympathetic). In addition, they used bilaterally GV 20 (middle of the skullpan), Extra 1 (middle between the eyebrows), and LI 4 (first dorsal interosseus muscle of the upper limbs)<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30-minute sessions, 5 times a week for 2 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Standard medication with carbamazepine to reduce withdrawal symptoms<br><br>**Comparator:** Sham acupuncture (superficial needling at Shen Men, Extra1, and LI4)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** *A priori* power calculation; targeted sample size achieved<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Clinical Institute Withdrawal Assessment (CIWA-Ar-scale) at postintervention, versus sham acupuncture: SMD −0.62, CI −1.31 to 0.07<br><br>**Functional status:** State-Trait Anxiety Inventory at postintervention, versus sham acupuncture: SMD −0.21, CI −0.89 to 0.46. Beck Depression Inventory at postintervention, versus sham acupuncture: SMD −0.50, CI −1.18 to 0.18. |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Killeen, et al., 2002<br><br>**References:** Killeen et al., 2002; Killeen, 1998<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Test the effectiveness of auricular acupuncture interventions in diminishing psychological and physiological changes associated with cocaine craving<br><br>**Quality rating:** Good<br><br>Comparable groups assembled with 100% follow-up, reliable measurement, interventions clearly described, ITT analysis used | **Number of patients:** 30 (15 acupuncture, 15 sham acupuncture)<br><br>**Baseline substance use:** Days used in the past month: 18.3 days (SD 8.8) for acupuncture, 17 days (SD 10) for sham acupuncture<br><br>**Comorbid psychological/behavioral health conditions:** Psychiatric diagnoses: 73% of acupuncture participants, 33% of sham acupuncture participants<br><br>**Age (Years):** Acupuncture: 37 (SD 4.7); sham acupuncture: 34 (SD 6.9)<br><br>**Gender:** 60% male<br><br>**Inclusion criteria:** Over the age of 18, (2) DSM-IV criteria for cocaine abuse or dependence; identify cocaine as their primary drug of abuse and reported cocaine use within the last 5 days; able to give adequate informed consent and function at a sufficient intellectual level<br><br>**Exclusion criteria:** Patients were excluded from the study if they were diagnosed with a DSM-IV psychotic disorder; taking medications specifically for craving; or dependent on substances other than nicotine or caffeine | **Content of acupuncture intervention:** Needles were inserted at NADA auricular acupoints (kidney, liver, lung, Shen Men, and sympathetic)<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** One 45-minute session<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** None reported<br><br>**Comparator:** Sham acupuncture (nonspecific auricular points)<br><br>**Primary endpoint:** Withdrawal at postintervention<br><br>**Power calculation:** *A priori* power calculation; targeted sample size achieved<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Cocaine Craving Questionnaire-Now (CCQ-Now) at postintervention, versus sham acupuncture: SMD 0.02, CI −0.69 to 0.74 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Konefal, Duncan, and Clemence, 1994<br><br>**References:** Konefal, Duncan, and Clemence, 1994<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Examine the feasibility of the use of acupuncture for substance abuse in a public health clinic setting<br><br>**Quality rating:** Poor<br><br>High attrition without ITT analysis | **Number of patients:** 568 (186 acupuncture, 194 TAU plus frequent urine testing, 188 TAU)<br><br>**Baseline substance use:** Primary drug: Alcohol: 14% acupuncture, 13% urine testing, 12% TAU; Marijuana: 11% acupuncture, 10% urine testing, 13% TAU; Cocaine: 24% acupuncture, 32% urine testing, 29% TAU; Crack: 44% acupuncture, 37% urine testing, 40% TAU; History of crack use: 51% acupuncture, 49% urine testing, 51% TAU<br><br>**Comorbid psychological/behavioral health conditions:** Psychiatric diagnoses: 73% of acupuncture participants, 33% of sham acupuncture participants<br><br>**Age (Years):** < 24: 21%; 25–34: 54%; 35+: 26%<br><br>**Gender:** 53% male<br><br>**Inclusion criteria:** Men and women between the ages of 18–65 years with a documented substance abuse problem<br><br>**Exclusion criteria:** None reported | **Content of acupuncture intervention:** Acupuncture at five ear points of NADA protocol (kidney, liver, lung, Shen Men, and sympathetic). Common withdrawal symptoms (e.g., stomach cramps, lower back pain, nightmares, insomnia, headaches, agitation, pain, and others) reported by the clients were treated using additional acupuncture points.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 2–5 times a week for 16 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** TAU plus frequent urine testing<br><br>**Comparator:** (1) Active comparator (frequent urine testing plus TAU); (2) TAU (16-week treatment program including individual counseling, sporadic urine testing mandated by the court (approximately once a month), and group sessions)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Treatment dropout:** Number of participants attending at least one session, versus active comparator: OR 1.14, CI 0.75 to 1.73; versus TAU: OR 0.72, CI 0.48 to 1.08 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Konefal, Duncan, and Clemence, 1995<br><br>**References:** Konefal, Duncan, and Clemence, 1995<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Examine the effects of three different treatments; one-needle auricular treatment, five-needle auricular treatment, and five-needle auricular treatment plus selected body points for self-reported symptoms<br><br>**Quality rating:** Poor<br><br>Relapse data not reported sufficiently for meta-analysis, ITT analysis not used | **Number of patients:** 321 (113 five-needle acupuncture, 110 five-needle acupuncture plus body points, 98 one-needle acupuncture)<br><br>**Baseline substance use:** Alcohol: 22.7%; Marijuana: 15.9%; Cocaine: 20.2%; Crack: 34.6%; None stated: 6.5%<br><br>**Comorbid psychological/behavioral health conditions:** Psychiatric diagnoses: 73% of acupuncture participants, 33% of sham acupuncture participants<br><br>**Age (Years):** < 24: 15%; 25–34: 50%; 35+: 35%<br><br>**Gender:** 69% male<br><br>**Inclusion criteria:** Self-referred or assigned by the court to undergo the outpatient drug counseling and substance abuse treatment program; between the ages of 18 and 65 years; documented substance abuse problem<br><br>**Exclusion criteria:** None reported | **Content of acupuncture intervention:** Five-needle auricular acupuncture according to the NADA protocol in a group setting<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 2–5 times a week for 16 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Standard outpatient care given by the Metro-Dade County Office of Rehabilitative Services, which includes individual counseling, court-mandated sporadic urine testing (approximately once a month), and group sessions<br><br>**Comparator:** (1) Five-needle auricular acupuncture (NADA protocol) plus body points for specific symptomatic treatment of complaints reported by the client; (2) one-needle auricular acupuncture (Shen Men point)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Treatment dropout:** 107 participants (94.7%) of the five-needle acupuncture group, 105 participants (95.5%) of the five-needle acupuncture plus body points group, and 94 participants (95.9%) of the one-needle acupuncture group completed at least one treatment session |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Kunz et al., 2007<br><br>**References:** Kunz et al., 2007<br><br>**Country:** Germany<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Investigate the hypothesis that acupuncture more than aromatherapy reduces withdrawal symptoms and shows specific effects<br><br>**Quality rating:** Fair<br><br>32% attrition but ITT analysis used, comparable groups at baseline, reliable measurement, withdrawal data not reported sufficiently | **Number of patients:** 109 (55 acupuncture, 54 aromatherapy)<br><br>**Baseline substance use:** Duration of dependence (years): 15.6 for acupuncture, 12.8 for aromatherapy control; Number of detoxifications: 23.9 for acupuncture, 25.9 for aromatherapy<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** Acupuncture: 47.9 (SD 9.8); aromatherapy: 43.8 (SD 7.0)<br><br>**Gender:** 82% male<br><br>**Inclusion criteria:** Patients who had been drinking within at least 10 days before enrollment; ICD-10 criteria for alcohol dependence<br><br>**Exclusion criteria:** Refusal to be randomized; current drug abuse; pregnancy; clinically evident cognitive impairment unrelated to current alcohol intoxication; active psychotic status; current additional medical conditions requiring treatment; severe coagulation disturbances; under 18 years old; patients with breath alcohol concentrations higher than 43.4 millimoles per liter to avoid invalid informed consents because of insufficient cognitive condition | **Content of acupuncture intervention:** Auricular acupuncture according to NADA protocol by psychiatrists or by mental-health nurses who were trained by a member of NADA<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 5 times a week for 1 week<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Routine treatment of alcohol, including prescription of carbamazepine, or oxcarbazepine and benzodiazepines, prescribed on an individual basis according to the alcohol-withdrawal syndrome scale scores. In case of uneasiness, patients had the option to take promethazine up to 100 mg/day in addition to standardized medication treatment.<br><br>**Comparator:** Active comparator (aromatherapy by an experienced aromatherapist)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** *A priori* power calculation; targeted sample size achieved<br><br>**Follow-up:** Postintervention | **Treatment dropout:** Number of participants who completed treatment, versus active comparator: OR 1.25, CI 0.56 to 2.81<br><br>**Adverse events:** Six participants (10.9%) in the acupuncture group self-reported negative side effects (e.g., pain and mild bleeding). Five participants (9.3%) in the aromatherapy group self-reported negative side effects (e.g., agitation, sneezing, negative thoughts, and sore throat). |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Lee et al., 2014<br><br>**References:** Lee et al., 2014<br><br>**Country:** South Korea<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:**<br>To examine the effect of acupuncture on Zhubin (KI9) in reducing alcohol craving in alcohol-dependent patients<br><br>**Quality rating:** Fair<br><br>Comparable groups, many important outcomes not considered | **Number of patients:** 20 (10 acupuncture, 10 sham acupuncture)<br><br>**Baseline substance use:** Number of drinking days per month: 16.3 (8.6) for acupuncture; 22.0 (10.4) for sham acupuncture; Number of drinks per drinking day: 13.8 (3.6) for acupuncture; 10.3 (6.2) for sham acupuncture; Duration of alcohol dependence (years): 7.4 (6.6) for acupuncture; 8.8 (4.4) for sham acupuncture<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** Acupuncture: 43 (SD 6.8); sham acupuncture: 44.5 (SD 7.9)<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** Met DSM-IV criteria for alcohol dependence, as diagnosed by two psychiatrists<br><br>**Exclusion criteria:** Current drug abuse other than alcohol, tobacco, or caffeine; clinically evident cognitive impairment; current medical and neurological disorders; history of another Axis I disorder; current use of psychotropic medications | **Content of acupuncture intervention:** TCM acupuncture at Zhubin (KI9). Needles were 0.25 x 0.40 mm. Acupuncture procedures were performed by an oriental-medical doctor who had graduated from an oriental-medical school in South Korea and had a license for oriental-medicine. Did not report if in a group setting.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 15-minute sessions, 2 times a week for 4 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Standard care at the hospital, which included group therapy and an education program<br><br>**Comparator:** Sham acupuncture (superficial insertion at the same acupoint as the acupuncture group)<br><br>**Primary endpoint:** Postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Withdrawal/craving:** Visual analog scale, versus sham acupuncture: SMD −1.48, CI −2.47 to 0.49<br><br>**Adverse events:** No participant reported definite complaints or side effects caused by acupuncture treatment |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Leung, 1977<br><br>**References:** Leung, 1977<br><br>**Country:** Canada<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Examine the effectiveness of acupuncture in treating withdrawal symptoms due to narcotics, alcohol, and other drugs<br><br>**Quality rating:** Poor<br><br>Unable to assess baseline comparability or reliability of measures, many important outcomes not considered, ITT analysis not used in small sample of 17 | **Number of patients:** 17 (8 acupuncture, 9 sham acupuncture)<br><br>**Baseline substance use:** 9 narcotic addicts, 5 alcohol addicts, and 3 addicted to other drugs<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** 39.8<br><br>**Gender:** 63% male<br><br>**Inclusion criteria:** Narcotic, alcohol, or barbiturates/valium addicts; 16+ years of age; well motivated to quit the drug<br><br>**Exclusion criteria:** No serious physical or psychiatric disorder; existing pregnancy | **Content of acupuncture intervention:** Lung point of the ear, and Spleen 6 was chosen as the auxiliary somatic point, which supposedly controls, among other things, gastrointestinal upsets and insomnia. The needle was inserted into this point through a hole in a piece of plastic tape without going through a piece of sponge adhered to the underside of the tape; the tape was used to wrap around the lower leg at the site of the SP-6 area. All needles were inserted bilaterally and connected by wires to an acupuncture stimulator. The machine was switched on, and current was passed through the needles.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 20-minute sessions, 11 times a week for 1 week<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** None reported<br><br>**Comparator:** Sham acupuncture (both nonspecific and superficial needling)<br><br>**Primary endpoint:** Withdrawal/craving at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Number of participants with no improvement of withdrawal symptoms at postintervention, versus sham acupuncture: SMD −0.66, CI −1.76 to 0.43 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Liang, et al., 2012<br><br>**References:** Liang, et al., 2012<br><br>**Country:** China<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Observe and analyze the intervention effects of needling different points for postwithdrawal syndrome of heroin dependence<br><br>**Quality rating:** Fair<br><br>ITT analysis not used (though only 3% attrition) | **Number of patients:** 62 (21 acupuncture, 21 active acupuncture comparator, 20 passive comparator)<br><br>**Baseline substance use:** Dependent on opioids<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** 39 (SD 8)<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** Met ICD-10 diagnostic criteria for opioid dependence; a history of drug addiction for more than 6 months, at a daily dose above 0.5 g; aged between 18 and 60 years old; presented significant postwithdrawal symptoms following 1-week detoxification; negative result of morphine urine screen test; discontinued any other therapies or drugs that may affect the assessment for this study<br><br>**Exclusion criteria:** Experiencing severe heart, liver and kidney damage; blood or respiratory system diseases; severe mental disorders; severe unhealed trauma; contagious diseases, such as liver problems or HIV/AIDS; women during pregnancy or breast feeding; severe digestive system diseases; severe malnutrition | **Content of acupuncture intervention:** Bilateral acupoints at Neiguan (PC 6) using disposable needles (with tube) of 0.22 mm in diameter and 25 mm in length, and apply even reinforcing-reducing manipulation upon arrival of qi. Manipulated for 2 minutes for each point until the presence of a local sore, numb, heavy, or distending sensation.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 20-minute sessions, 3 times a week for 4 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** None reported<br><br>**Comparator:** (1) Active acupuncture comparator (bilateral acupoints at Bilateral Shen Men (HT 7)); (2) passive comparator (no intervention)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Self-reported postwithdrawal symptoms at postintervention, versus passive comparator: SMD −1.04, CI −1.71 to −0.38<br><br>**Functional status:** Hamilton Anxiety Scale at postintervention, versus passive comparator: SMD −1.09, CI −1.76 to −0.42<br><br>**Treatment dropout:** Number of participants who completed treatment, versus passive comparator: OR 3.00, CI 0.12 to 78.04 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Lipton, Brewington, and Smith, 1994<br><br>**References:** Lipton, Brewington, and Smith, 1994<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Evaluate the efficacy of acupuncture for cocaine/crack abuse<br><br>**Quality rating:** Poor<br><br>High selection bias, assembled groups differ in heroin use, unreliable measures of craving/withdrawal, ITT analysis not used | **Number of patients:** 150 (73 acupuncture, 77 sham acupuncture)<br><br>**Baseline substance use:** Number of days that the subject used cocaine in the month before treatment: Smoked on average: 19.6 (SD 9.11) days in acupuncture group, 20.1 (SD 8.5) days in sham acupuncture group; Injected on average: 1.5 days in acupuncture group, 1.9 days in sham acupuncture group<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** Acupuncture: 30.3, sham acupuncture: 29.9<br><br>**Gender:** 72% male<br><br>**Inclusion criteria:** Age 18 or over; cocaine/crack smoking or intravenous cocaine use as primary substance abuse problem; use of cocaine/crack at least 3 days in the previous week; no prior experience with any type of acupuncture therapy; no serious back pain problems<br><br>**Exclusion criteria:** Prior experience with any type of acupuncture therapy; serious back pain problems | **Content of acupuncture intervention:** Acupuncture bilaterally at four ear points specifically related to detoxification (liver, lung, Shen Men, and sympathetic)<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 1–7 times a week for 4.5 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** None reported<br><br>**Comparator:** Sham acupuncture (nonspecific points)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 2 months | **Relapse:** Percentage of urine samples that were cocaine-negative at postintervention, versus sham acupuncture: SMD −0.06, CI −0.40 to 0.28<br><br>**Treatment dropout:** Number of participants who attended 10 sessions, the minimal number of treatment recommended, versus sham acupuncture: OR 1.22, CI 0.63 to 2.36 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Lua and Talib, 2013<br><br>**References:** Lua and Talib, 2013; Lua, Talib, and Ismail, 2013<br><br>**Country:** Malaysia<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Compare the clinical outcomes of methadone maintenance treatment (MMT) alone and MMT plus AA (MMT+AA)<br><br>**Quality rating:** Poor<br><br>More than 20% attrition, ITT analysis not used, initially assembled groups were not comparable on almost a dozen variables | **Number of patients:** 97 (55 acupuncture, 42 drug therapy)<br><br>**Baseline substance use:** 54.6% of participants used opioids; 25% of participants were abusing miscellaneous substances such as benzodiazepine, amphetamine-type stimulants (ATSs), and cannabis; Daily methadone dose (mg): 58.87 ± 19.11 for acupuncture, 55.38 ± 22.20 for drug therapy<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** 37.7<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** Dependence on opiates as established by the physician in charge through the Opiate Treatment Index and a scheduled urinary drug test; volunteered to participate in the MMT program; 18 years of age or older; understand, read, speak, and write in the Malay language; be capable of answering questions either in written form or by interview<br><br>**Exclusion criteria:** Exhibited violent behaviors, suicidal tendencies, or psychotic profiles; infected with HIV or hepatitis B; was allergic to metal; displayed rude behaviors and was involved in criminal activities | **Content of acupuncture intervention:** Auricular acupuncture according to NADA protocol bilaterally at five ear points (kidney, liver, lung, Shen Men, and sympathetic). Needles were inserted to a depth of 1 to 3 mm, without applying any electrical stimulation or vibration. Acupuncture treatments were delivered in a group setting by an experienced acupuncturist.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 3<br><br>**Dosage:** 30-minute sessions, 3 times a week for 8 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Standard methadone treatment (required to undergo a urine drug test every 2 weeks to detect relapse (total = five tests). Initiated on a methadone dose of between 15 and 20 mg upon admission, and this dosage was gradually increased according to their individual needs.<br><br>**Comparator:** Active comparator (drug therapy; see co-intervention)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Overall withdrawal symptoms at postintervention, versus active comparator: SMD −0.15, CI −0.33 to 0.63<br><br>**Relapse:** Number of participants with positive urine drug tests at postintervention, versus active comparator: SMD 0.38, CI −0.50 to 1.25<br><br>**Health-related quality of life:** Total Score on Malay World Health Organization Quality of Life (WHOQOL-BREF) scale, versus active comparator: SMD −0.15, CI −0.45 to 0.15<br><br>**Recovery outcomes:** 2 participants were imprisoned (do not know which group)<br><br>**Adverse events:** Participants in the acupuncture group experienced the following adverse events: dizziness (65.5%), tingling sensation (65.5%), nausea (65.5%), slight fever (65.5%), light headache (58.6%), pain (58.6%), dry mouth (51.7%), slight bleeding (48.3%), and drowsiness (37.9%). This information was not collected/reported for the active comparator group. |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Man and Chuang, 1980<br><br>**References:** Man and Chuang, 1980<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Test the efficacy of acupuncture in methadone withdrawal<br><br>**Quality rating:** Poor<br><br>Unreliable measurements used, large attrition, inability to detect whether ITT analysis was used, no outcomes reported sufficiently to make group comparisons | **Number of patients:** 35 (number randomized to each condition not clear)<br><br>**Baseline substance use:** Drug abuse history of 5–20 years, with a mean of 10 years<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** 32.4<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** Healthy male veterans with a long history of drug abuse, particularly heroin; on a methadone maintenance program and admitted to the drug unit (a methadone detoxification ward where the patients were treated for a period of 2–3 months)<br><br>**Exclusion criteria:** None reported | **Content of acupuncture intervention:** Two acupuncture needles were placed in each ear at the lung and stomach point. Needles were connected to an electroacupuncture machine, which delivered a current of 2 milliampere at 6,000 c/m with 10 Km. The intensity of the current was gradually increased stepwise according to the tolerance of the patient. All patients were treated by the same experienced acupuncturist.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 3<br><br>**Dosage:** 30-minute sessions, 7 times a week for 4 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Active intervention (methadone detoxification)<br><br>**Comparator:** Active intervention (methadone detoxification)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 3 months | **Relapse:** Six patients (3 in acupuncture, 3 in methadone control) finished treatment with drug-free urine samples |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Margolin, Kleber, et al., 2002<br><br>**References:** Kleber, 1997; Margolin, Avants, and Kleber, 1998; Margolin, Kleber, et al., 2002<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Investigate the effectiveness of auricular acupuncture as a treatment for cocaine addiction<br><br>**Quality rating:** Fair<br><br>Acceptable measurement, differences between completers and noncompleters, ITT analysis used | **Number of patients:** 620 (222 acupuncture, 203 sham acupuncture, 195 passive comparator)<br><br>**Baseline substance use:** Used cocaine for an average of 10.94 (SD 7.10) years<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** 38.80 (SD 7.60)<br><br>**Gender:** 69% male<br><br>**Inclusion criteria:** At least 18 years of age; DSM-IV SCID (Structured Clinical Interview); evidence of recent cocaine use either by providing a cocaine-positive urine screen at or within 2 weeks before screening or by self-reporting cocaine use in the week before screening<br><br>**Exclusion criteria:** Dependent on any substance besides opiates, cocaine, or nicotine; currently receiving treatment for cocaine dependence; currently taking a prescription benzodiazepine; currently taking any other psychotropic medication unless maintained on this medication for at least 90 days; currently receiving acupuncture treatment or having had acupuncture in the previous 30 days; being actively suicidal or psychotic | **Content of acupuncture intervention:** Needles inserted into the auricles bilaterally at four ear points (liver, lung, Shen Men, and sympathetic). Stainless steel needles were 0.2 mm wide and 15.0 mm long.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 6<br><br>**Dosage:** 40-minute sessions, 5 times a week for 8 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Concurrent drug counseling. At the primary cocaine sites, patients were offered weekly individual counseling sessions according to a treatment manual that was developed for this study and focused on changing addictive behaviors. Methadone-maintained patients continued to receive standard methadone maintenance, which included drug counseling.<br><br>**Comparator:** (1) Sham acupuncture (nonspecific points); (2) Passive comparator (relaxation videos and soft music)<br><br>**Primary endpoint:** Relapse and treatment dropout at 6-month follow-up<br><br>**Power calculation:** *A priori* power calculation; targeted sample size achieved<br><br>**Follow-up:** 6 months | **Relapse:** Percentage of urine samples testing positive during treatment, versus sham acupuncture: SMD 0.12, CI −0.17 to 0.40; versus passive comparator: SMD 0.14, CI −0.15 to 0.43. Rates of abstinence at six-month follow-up, versus sham acupuncture: SMD 0.07, CI −0.23 to 0.37; versus passive comparator: SMD −0.19, CI −0.50 to 0.12.<br><br>**Treatment dropout:** Number of participants who completed treatment, versus sham acupuncture: OR 1.03, CI 0.70 to 1.51; versus passive comparator: OR 0.96, CI 0.65 to 1.42 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Margolin, Avants, and Arnold, 2005<br><br>**References:** Margolin, Avants, and Arnold, 2005<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Examine differences between the standard five-needle NADA auricular acupuncture protocol and a reduced needle protocol<br><br>**Quality rating:** Good<br><br>Reliable measurement, clearly described interventions, ITT analysis used | **Number of patients:** 40 (20 acupuncture, 20 active acupuncture comparator)<br><br>**Baseline substance use:** Used opiates for 21.32 (± 9.2) years and cocaine for 18.07 (± 7.93) years<br><br>**Comorbid psychological/behavioral health conditions:** All participants were HIV seropositive; 30% were asymptomatic, 45% were symptomatic, and 20% met U.S. Centers for Disease Control and Prevention criteria for AIDS<br><br>**Age (Years):** 42.83 (SD 7.4)<br><br>**Gender:** 60% male<br><br>**Inclusion criteria:** Being treated at an inner-city methadone maintenance program; confirmed HIV-seropositive status, opioid dependence, and abuse or dependence on cocaine<br><br>**Exclusion criteria:** None reported | **Content of acupuncture intervention:** Auricular acupuncture according to NADA protocol at five ear points (kidney, liver, lung, Shen Men, and sympathetic). Needles were 0.20 mm wide and 15 mm long, inserted into the cartilage to a depth of 1–3 mm.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** Sessions 5 times a week for 8 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Standard methadone treatment, which included daily methadone, tailored to each patient's need (average dose, 88.5 (± 15.9) mg/day). The last 15 participants in the study also received Spiritual Self-Schema therapy, which aims to decrease the habitual activation of the ""addict"" self-schema and to create, strengthen, and activate a personally meaningful spiritual self-schema that is compatible with HIV-preventive behavior.<br><br>**Comparator:** Modified NADA protocol with 1–3 needles (lung, Shen Men, and sympathetic)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Functional status:** Beck Depression Inventory at postintervention, versus modified NADA protocol: SMD 0.12, CI −0.50 to 0.74; State-Trait Anxiety Inventory at postintervention, versus modified NADA protocol: SMD 0.38, CI −0.25 to 1.00 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Montazeri, Farahnakian, and Saghaei, 2002<br><br>**References:** Montazeri, Farahnakian, and Saghaei, 2002<br><br>**Country:** Iran<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Evaluate the effect of acupuncture on the severity of withdrawal reaction during rapid opiate detoxification<br><br>**Quality rating:** Fair<br><br>Comparable groups, 100% follow-up, self-reported withdrawal symptoms reported insufficiently for meta-analysis | **Number of patients:** 40 (20 acupuncture, 20 drug therapy)<br><br>**Baseline substance use:** Abused agent: Opium: 50% acupuncture participants, 65% drug therapy participants; Heroin: 50% acupuncture, 35% drug therapy. Addiction duration: 3.5 years (SD 1.8) for acupuncture, 3.8 (SD 2) for drug therapy. Age when became addicted: 30 years (SD 6) for acupuncture; 30 years (SD 5) for drug therapy. Heroin intake (g/day): 1.2 (SD 0.2) for acupuncture; 1.1 (SD 0.3) for drug therapy. Opium intake (g/day): 4 (SD 1.2) for acupuncture; 3.8 (SD 1.5) for drug therapy.<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** Acupuncture: 32 (SD 8), drug therapy: 31 (SD 9)<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** Male adults addicted to heroin or opium who were referred to the University Rehabilitation Center for the drug abuse<br><br>**Exclusion criteria:** Patients with history of addiction less than 6 months; history of cardiovascular, renal, psychiatric, and severe respiratory disorders | **Content of acupuncture intervention:** Needle acupuncture, using gauge 30 disposable acupuncture needles, on the following acupoints: LI4 (analgesia); PC6 and ST36 (treatment of nausea, vomiting, and abdominal discomfort); HT7 and LR3 (treatment of restlessness); DU14 (an important governing and coordinating point); and DU20 (harmonizing effect). Manual stimulation involved rotating the needle evenly and gently clockwise and counterclockwise, performed every 10 minutes for 3 hours<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 3 times a week for 1 week<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Rapid opioid detoxification for a 10-day period, beginning with an abstinence period of 24 hours<br><br>**Comparator:** Active comparator (drug therapy; see co-intervention)<br><br>**Primary endpoint:** Withdrawal at postintervention<br><br>**Power calculation:** *A priori* power calculation; targeted sample size achieved<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Number of participants who needed adjuvant drugs to help with withdrawal/craving at postintervention, versus active comparator: SMD −1.21, CI −2.15 to −0.27<br><br>**Adverse events:** There was no recorded clonidine-associated side effect. After diazepam administration, a few patients required a brief period of assisted ventilation with a mask, but no patients developed hypoxia. Neither pulminary edema nor other severe side effects attributable to naloxone administration was observed. |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Mu et al., 2013<br><br>**References:** Mu et al., 2013<br><br>**Country:** China<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Observe the effect of electroacupuncture at Jiaji (EX-B 2) points for anxiety and craving in heroin addicts during detoxification<br><br>**Quality rating:** Fair<br><br>Comparable groups, reliable measurement, ITT analysis used, some but not all important outcomes considered | **Number of patients:** 60 (30 acupuncture, 30 drug therapy)<br><br>**Baseline substance use:** Heroin addiction<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** 32.51 (SD 6.35)<br><br>**Gender:** 58% male<br><br>**Inclusion criteria:** DSM-IV criteria for opioid withdrawal; positive urine drug test for opioids or positive naloxone challenge test (NCT) withdrawal symptoms and cravings (e.g., generalized body ache, anxiety, and insomnia); a history of drug use for 3 months or longer and daily drug dose of less than 3 g/day; aged between 18 and 55 years old; having received no other detoxification therapies during the past 3 months<br><br>**Exclusion criteria:** Complications of severe organic diseases involving heart, liver, and kidney; severe primary hematopoietic system conditions; psychotic patients; complications of pulmonary tuberculosis and HIV infection; severe malnutrition subjects; women during lactation or pregnancy; failure to cooperate; involvement in other drug experiments | **Content of acupuncture intervention:** Treated with electroacupuncture bilaterally at Jiaji (EX-B 2) points at the level of T5-7 and Shenshu (BL23). Needles were 0.35 mm in diameter and 40 mm in length. Upon arrival of needling sensation, acupuncturists connected Jiaji (EX-B 2) points at the level of T7 and Shenshu (BL23) on the same side with a G6805-2 low-frequency electronic impulse device, using a sparse wave, with frequency of 5 Hz and stimulation intensity of 5 milliamperes<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 20-minute sessions, 5–7 times a week for 2 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Methadone and doxepin for two weeks: 10 mg of methadone for each dose, 3 doses a day; 25 mg of doxepin for each dose, 3 doses a day<br><br>**Comparator:** Active comparator (drug therapy; see co-interventions)<br><br>**Primary endpoint:** Anxiety at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Functional status:** Self-Rating Anxiety Scale at postintervention, versus active comparator: SMD −0.80, CI −1.33 to −0.27 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Otto, Quinn, and Sung, 1998<br><br>**References:** Otto, Quinn, and Sung, 1998<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Determine whether auricular acupuncture might enhance standard treatment for cocaine-dependent veterans<br><br>**Quality rating:** Poor<br><br>Large attrition, small number of participants, limited to no actual data reported on outcome measures or their differences | **Number of patients:** 36 (25 acupuncture, 11 sham acupuncture)<br><br>**Baseline substance use:** Some participants had a previous history of abuse or dependence on other substances, but these had been in remission for several years by the time of this admission to the Department of Veterans Affairs (VA) medical facility<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** 38.9<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** DSM-III-R criteria for cocaine dependence<br><br>**Exclusion criteria:** Acute medical problems; current psychiatric comorbidity; met criteria for current dependence on other psychoactive substances | **Content of acupuncture intervention:** Auricular acupuncture bilaterally at five ear points (kidney, liver, lung, Shen Men, and sympathetic). Needles inserted to a depth of approximately 0.5 mm. Acupuncture treatment delivered in a group setting by trained acupuncturist.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30- to 45-minute sessions, 1–5 times a week for 12 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Full daily schedule of group meetings, chores, and recreational pursuits<br><br>**Comparator:** Sham acupuncture (points close to but distinct from the substance abuse sites: sciatic nerve and knee, plus lumbosacral, dorsal, and cervical vertebrae points)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Relapse:** Number of participants who relapsed during inpatient treatment, versus sham acupuncture: SMD −0.92, CI −2.32 to 0.47<br><br>**Treatment dropout:** Number of participants who completed the final treatment phase, versus sham acupuncture: OR 0.73, CI 0.07 to 7.95<br><br>**Adverse events:** Some participants reported pain from or fear of needles (do not know which group) |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Pirmoradi and Abdollahi, 2008<br><br>**References:** Pirmoradi and Abdollahi, 2008<br><br>**Country:** Iran<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Investigate the effect of acupuncture on the treatment of drug abuse<br><br>**Quality rating:** Poor<br><br>Authors did not provide sufficient information about follow-up, ITT analysis, or measurement instruments. Only "improvement in addiction symptoms" was measured, with no further explanation about this measure. | **Number of patients:** 96 (48 acupuncture, 48 drug therapy)<br><br>**Baseline substance use:** Not reported<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** Not reported<br><br>**Gender:** 92% male<br><br>**Inclusion criteria:** Heroin/opium addiction<br><br>**Exclusion criteria:** None reported | **Content of acupuncture intervention:** Electroacupuncture bilaterally in five ear points (kidney, liver, lung, Shen Men, and sympathetic) and other body areas (LI4 (Hegu), HT7 (Shen Men), PC6 (Neiguan), ST36 (Zusanli), LR3 (Taichong), and Back-shu points involving the heart, kidneys, liver, lungs, and spleen). Needles were gauge 13 for the ears and gauge 25 and 40 for the other body areas.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30- to 45-minute sessions, 1–21 times a week for 32 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Psychological interventions, including psychotherapy, group therapy, and family education<br><br>**Comparator:** Active comparator (drug therapy: methadone or clonidine, along with other supplementary drugs such as tranquilizers)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 9 months | **Withdrawal/craving symptoms:** Number of participants who showed "improvement" in addiction symptoms at postintervention, versus active comparator: SMD −0.66, CI −1.33 to 0.02; and at three-month follow-up, versus active comparator: SMD −0.58, CI −1.05 to −0.12 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Rampes et al., 1997<br><br>**References:** Rampes et al., 1997<br><br>**Country:** United Kingdom<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Determine whether auricular electroacupuncture reduces craving for alcohol<br><br>**Quality rating:** Poor<br><br>56% attrition with no ITT analysis | **Number of patients:** 59 (23 acupuncture, 20 sham acupuncture, 16 TAU)<br><br>**Baseline substance use:** Dependence on or abuse of alcohol<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** Acupuncture: 38.3 (SD 10.8); sham acupuncture: 39.9 (SD 10.8); TAU: 41.6 (SD 11.6)<br><br>**Gender:** Acupuncture: 83% male; sham acupuncture: 85% male; TAU: 63% male<br><br>**Inclusion criteria:** Aged between 18 and 65; fulfilling alcohol-dependence or abuse criteria; attended initial assessment<br><br>**Exclusion criteria:** No craving; were pregnant; had a pacemaker; had previous acupuncture; were taking any psychotropic medication | **Content of acupuncture intervention:** Electroacupuncture bilaterally on three ear sites (lung, Shen Men, and sympathetic). Needles were 15 mm length and 0.22 mm diameter. Needles were not manipulated following insertion. The leads were looped over the ear and taped to the neck of the patient. A square-wave continuous electric current of 100 Hz frequency was applied. The current was slowly increased until the patients felt either a tingling sensation or a warm sensation at one or both of the needles connected.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30-minute sessions, 1 time a week for 6 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Initial assessment by and allocation to community alcohol team counselor, and attendance for group therapy; home/inpatient detoxification and referrals to rehabilitation hostels<br><br>**Comparator:** (1) Sham acupuncture (nonspecific points); (2) TAU (see co-interventions)<br><br>**Primary endpoint:** Withdrawal/craving (follow-up not specified)<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 3 months | **Quantity of substance use:** Breathalyzer alcohol level at 0.5 months postintervention, versus sham acupuncture: SMD 0.16, CI −0.69 to 1.02; versus TAU: SMD 0.36, CI −0.72 to 1.44<br><br>**Withdrawal/craving symptoms:** Craving for alcohol in the previous week, using the visual analog scale, at 0.5 months postintervention, versus sham acupuncture: SMD −0.11, CI −0.95 to 0.73; versus TAU: SMD −2.25, CI −3.63 to −0.87. Craving for alcohol in the previous week, using the visual analog scale, at three-month follow-up, versus sham acupuncture: SMD 0.24, CI −0.61 to 1.08; versus TAU: SMD −0.33, CI −1.47 to 0.81.<br><br>**Functional status:** Clinical Anxiety Scale at 0.5 months postintervention, versus sham acupuncture: SMD 0.11, CI −0.76 to 0.97; versus TAU: SMD −1.40, CI −2.71 to −0.08; and at three-month follow-up, versus TAU: SMD −1.15, CI −2.38 to 0.07.<br><br>**Recovery outcomes:** Some participants dropped out due to incarceration (do not know which group)<br><br>**Adverse events:** One participant (5.0%) in the sham acupuncture group withdrew from treatment due to pain from treatment. There was also slight bleeding at the site of needle insertion, as well as nausea, for some participants (do not know which group). |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Richard et al., 1995<br><br>**References:** Richard et al., 1995<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Assess whether acupuncture, anticraving medication, or brainwave modification improve outcomes of an intensive outpatient program for crack cocaine users<br><br>**Quality rating:** Poor<br><br>Key outcomes not reported sufficiently for meta-analysis, ITT analysis not used | **Number of patients:** 186 (41 acupuncture, 40 drug therapy, 57 brain wave modification, 48 TAU)<br><br>**Baseline substance use:** Not reported<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** 18–25: 19.3%; 26–30: 28.5%; 31–35: 25%; 36–40: 17.1%; 41–51: 10.1%<br><br>**Gender:** 62% male<br><br>**Inclusion criteria:** Reside in Harris County, Texas; have a diagnosis of crack cocaine addiction as determined by a state-certified admissions counselor; minimum age of 18 years<br><br>**Exclusion criteria:** Refusal to provide sufficient relocation follow-up information | **Content of acupuncture intervention:** Auricular acupuncture at five ear points for drug detoxification. Acupuncture was delivered by four state-certified counselors who had been trained and certified as acupuncture detoxification specialists.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30-minute sessions, 3–7 times a week for 4.5 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Neurobehavioral group and individual counseling therapies focusing on environmental cues that trigger cravings for cocaine, training the client to recognize and counteract such cues, and client recognition of addictive behaviors through guided peer interaction<br><br>**Comparator:** (1) Active comparator (drug therapy: anticraving medication); (2) active comparator (brainwave modification: biofeedback training); (3) TAU (see co-interventions)<br><br>**Primary endpoint:** Treatment dropout at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 8 months | **Treatment dropout:** Number of participants retained in treatment 31+ days, versus drug therapy: OR 0.41, CI 0.16 to 1.02; versus TAU: OR 1.33, CI 0.58 to 3.09 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
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| **Parent study:** Sapir-Weise et al., 1999<br><br>**References:** Sapir-Weise et al., 1999<br><br>**Country:** Sweden<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Evaluate whether acupuncture on correct points had better compliance, less craving, and less drinking than those receiving it on the incorrect points<br><br>**Quality rating:** Fair<br><br>Comparable groups assembled, ITT analysis used, data missing on collected outcomes (such as frequency of substance use) | **Number of patients:** 72 (36 acupuncture, 36 sham acupuncture)<br><br>**Baseline substance use:** Alcohol Use Inventory Scores (decentiles based on national norms, mean) for alcohol abuse: 7 (SD 3.1) for acupuncture, 7.4 (SD 2.6) for sham acupuncture<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** 45 (SD 9)<br><br>**Gender:** 71% male<br><br>**Inclusion criteria:** Alcohol-dependent according to DSM-III-R and based on the SCID<br><br>**Exclusion criteria:** Pregnancy, diabetes mellitus; thrombocytopenia; metal allergy; present warfarin or analgesic medication | **Content of acupuncture intervention:** Auricular acupuncture bilaterally in three ear points (lung, Shen Men, and sympathetic). Acupuncture was delivered in a group setting by a male registered nurse (RSW) trained in acupuncture.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 45-minute sessions, 2–5 times a week for 10 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Mainly social support and aversive treatment with disulfiram or calcium carbide<br><br>**Comparator:** Sham acupuncture (nonspecific ear points, located 3–5 mm from the specific points)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 6 months | **Quantity of substance use:** Number of participants with successful drinking pattern, which was limited days of alcohol misuse, defined as consumption of > 60 g of alcohol, at 0.5-month follow-up, versus sham acupuncture: SMD −0.06, CI −0.57 to 0.45; and at 3.5-month follow-up, versus sham acupuncture: SMD 0.22, CI −0.34 to 0.79<br><br>**Withdrawal/craving symptoms:** Number of participants with slight to no craving at 0.5 months postintervention, versus sham acupuncture: SMD 0.25, CI −0.27 to 0.77; and at 3.5-month follow-up, versus sham acupuncture: SMD −0.06, CI −0.58 to 0.46<br><br>**Treatment dropout:** Number of participants who completed the final phase of treatment, versus sham acupuncture: OR 0.51, CI 0.20 to 1.30 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Song, Hu, et al., 2010<br><br>**References:** Song, Hu, et al., 2010<br><br>**Country:** China<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Observe the clinical efficacy of combined acupuncture and psychological desensitization therapy for anxiety in those with heroin addiction<br><br>**Quality rating:** Fair<br><br>Comparable on reported baseline measures, reliable instruments, some but not all important outcomes were considered, ITT analysis used | **Number of patients:** 90 (45 acupuncture, 45 passive comparator)<br><br>**Baseline substance use:** More than 5 months of heroine withdrawal<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** Acupuncture: 33.38 (SD 6.39); passive comparator: 35.36 (SD 6.86)<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** DSM-III diagnosis of opioid dependence; urine test negative for morphine<br><br>**Exclusion criteria:** Mental disorders; life-threatening primary conditions (e.g., cardio-cerebrovascular disease); severe problems involving liver, kidney, and hematopoietic system; antianxiety or antidepression therapy within 1 month; in critical conditions that are too difficult for an accurate evaluation on the efficacy and safety | **Content of acupuncture intervention:** Acupuncture at Baihui (GV 20) and Neiguan (PC 6) (alternating two sides, selecting one side each time). Punctured Baihui (GV 20) 10 mm subcutaneously and Neiguan (PC 6) 15–20 mm perpendicularly, followed by even reinforcing-reducing manipulation within the patients' tolerance. Also applied moxibustion to Zusanli (ST 36). The needles were manipulated twice during each session.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30-minute sessions, 2 times a week for 8 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Psychological desensitization therapy (exposure to a heroin-related environment, bringing the patients into contact with multiple drugs, including heroin in glass bottles)<br><br>**Comparator:** Passive comparator (no treatment reported)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Visual analog scale at postintervention, versus passive comparator: SMD −1.36, CI −1.82 to −0.90<br><br>**Functional status:** Self-Rating Anxiety Scale at postintervention, versus passive comparator: SMD −0.98, CI −1.42 to −0.55 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Song, Li, et al., 2012<br><br>**References:** Song, Li, et al., 2012<br><br>**Country:** China<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Observe the influence of acupuncture on sleep disorders and anxiety in patients with heroin dependence<br><br>**Quality rating:** Fair<br><br>Comparable groups on reported measures, reliable assessment, some but not all important outcomes were considered, ITT analysis used | **Number of patients:** 62 (35 acupuncture, 27 passive comparator)<br><br>**Baseline substance use:** Heroin dependence<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** Acupuncture: 35.03 (SD 7.18); passive comparator: 34.15 (SD 5.64)<br><br>**Gender:** 100% male<br><br>**Inclusion criteria:** DSM-III diagnosis of opioid dependence; urine test negative for morphine<br><br>**Exclusion criteria:** Primary life-threatening diseases of the cardio-cerebrovascular, hepatic, renal, and/or hematopoietic systems; mental disorders; treated with antianxiety and antidepression agents within 1 month; in critical condition and difficult for precise assessment of the efficacy and safety | **Content of acupuncture intervention:** Needle acupuncture at Baihui (GV 20), Neiguan (PC 6), and Shen Men (HT 7) and moxibustion at Zusanli (ST 36). Needles of 0.35 mm in diameter and 40 mm in length were used. All needles were manipulated with moderate needling technique, in accordance with the patient's tolerance, once every 15 minutes. Moxibustion was applied to Zusanli (ST 36).<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30-minute sessions, 2 times a week for 8 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Not reported<br><br>**Comparator:** Passive comparator (no treatment reported)<br><br>**Primary endpoint:** Anxiety at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Functional status:** Self-Rating Anxiety Scale at postintervention, versus passive comparator: SMD −0.37, CI −0.87 to 0.14 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Toteva and Milanov, 1996<br><br>**References:** Toteva and Milanov, 1996<br><br>**Country:** Bulgaria<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Evaluate and compare the treatment efficacy of body acupuncture with conventional medical detoxification for subjects with alcohol dependence and withdrawal syndrome<br><br>**Quality rating:** Poor<br><br>Insufficient information about reliability/validity of measurement instruments provided, 70% attrition at follow-up, ITT analysis not used | **Number of patients:** 118 (50 acupuncture, 68 drug therapy)<br><br>**Baseline substance use:** Duration of alcohol dependence in the acupuncture treatment group was 5–13 years (mean 8.3). The duration of alcohol dependence was 5–14 years (mean 8.7 years) in the drug therapy group.<br><br>**Comorbid psychological/behavioral health conditions:** Not reported<br><br>**Age (Years):** Acupuncture: 32.3; drug therapy: 34.5<br><br>**Gender:** 76% male<br><br>**Inclusion criteria:** Meeting DSM-IV criteria for alcohol dependence; abstinence from alcohol for at least 10 days prior<br><br>**Exclusion criteria:** Resided in halfway houses; refused randomization; currently taking an alcohol deterrent (e.g., disulfiram/Antabuse) or other therapeutic drugs | **Content of acupuncture intervention:** Acupuncture delivered on the following points: LI-4 (Hegu), LI-11 (Quchi), PC-6 (Neiguan), SJ-5 (Waiguan), SI-4 (Wangu), GB-8 (Shuaigu), GB-14 (Yangbai), HT-7 (Shen Men), Taiyang (extra), and Yintang (extra). Points were varied at each session in different combinations of 5 or 6 bilateral points to avoid adaptation. 30-gauge needles, 1.5 inches in length, were inserted at depths appropriate to the particular point and patient's size. Acupuncture delivered by same licensed acupuncturist, experienced in addictionology. Subjects with a history of alcohol abuse greater than 10 years were given 15 minutes of electrostimulation twice per week.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 20- to 30-minute sessions, 7 times a week for 2 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Not reported<br><br>**Comparator:** Active comparator (drug therapy)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 6 months | **Relapse:** Number of participants in remission at six-month follow-up, versus active comparator: SMD −0.57, CI −1.36 to 0.22<br><br>**Functional status:** Self-reported improvement in depressive symptoms at postintervention, versus active comparator: SMD −1.41, CI −2.03 to −0.79<br><br>**Withdrawal/craving symptoms:** Decrease in desire for alcohol consumption at postintervention, versus active comparator: SMD −2.52, CI −3.64 to −1.39<br><br>**Treatment dropout:** Number of participants who completed treatment, versus active comparator: OR 0.13, CI 0.04 to 0.45 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Trumpler et al., 2003<br><br>**References:** Trumpler et al., 2003<br><br>**Country:** Switzerland<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Compare laser and needle acupuncture with a sham intervention for alcohol withdrawal<br><br>**Quality rating:** Fair<br><br>Unequal assessment of outcomes between groups, confounding at baseline (that was adjusted for in analyses), good retention, ITT analyses used | **Number of patients:** 48 (15 needle acupuncture, 17 laser acupuncture, 16 sham laser acupuncture)<br><br>**Baseline substance use:** All 48 patients were actively drinking at the time they were admitted<br><br>**Comorbid psychological/behavioral health conditions:** Depression: 33% acupuncture, 24% laser acupuncture, 38% sham laser acupuncture; Personality disorder: 27% acupuncture, 59% laser acupuncture, 56% sham laser acupuncture; Anxiety disorder: 27% acupuncture, 6% laser acupuncture, 38% sham laser acupuncture<br><br>**Age (Years):** Acupuncture: 45; laser acupuncture: 43; sham laser acupuncture: 49<br><br>**Gender:** 58% male<br><br>**Inclusion criteria:** DSM-IV criteria for alcohol dependence<br><br>**Exclusion criteria:** Current drug abuse; pregnancy; clinically evident cognitive impairment; current medical conditions requiring treatment; a history of schizophrenia; epilepsy or coagulation disturbances; current anticoagulation, age under 18 or over 65 years | **Content of acupuncture intervention:** Auricular acupuncture on two to ten (out of 24) prespecified ear points for chemical dependency, chosen individually at each session. Acupuncture treatment was delivered by one of two acupuncturists. Needles were 0.2 × 15 mm and inserted to a depth of 1–3 mm at ear points considered appropriate. Needles were twirled 180 degrees during insertion.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30- to 40-minute sessions, 7 times a week for 1 week<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Prescription of clomethiazole on an individual basis, with symptom-guided dosage. Patients could be prescribed benzodiazepines against withdrawal symptoms if it was considered appropriate by the treating psychiatrists.<br><br>**Comparator:** (1) Active comparator (laser acupuncture); (2) passive comparator (sham laser acupuncture)<br><br>**Primary endpoint:** Withdrawal/craving at 0.5-month follow-up<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 0.5 months | **Withdrawal/craving symptoms:** Time (days) to end of withdrawal, as measured by the Mainz Alcohol Withdrawal Scale (MAWS), at 0.5 months postintervention, versus active comparator: SMD −0.60, CI −1.31 to 0.11; versus passive comparator: SMD −0.43, CI −1.15 to 0.28<br><br>**Treatment dropout:** Number of participants who completed treatment, versus active comparator: OR 1.13, CI 0.02 to 60.37; versus passive comparator: OR 0.33, CI 0.01 to 8.83<br><br>**Adverse events:** Neither local side effects nor development of delirium tremens was reported for any participants. One participant in the auricular acupuncture group experienced self-limiting generalized convulsions of 5 minutes duration on the fifth day of withdrawal while she was sleeping; this was judged to be a withdrawal-related epileptic seizure on clinical grounds, and no epilepsy-specific potentials could be detected in a subsequent electroencephalogram. |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Washburn et al., 1993<br><br>**References:** Washburn et al., 1993<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Test whether standard acupuncture would have an effect on treatment retention and opiate use compared with sham/placebo<br><br>**Quality rating:** Fair<br><br>Large attrition for urine analysis, but ITT analysis used; comparable groups at baseline; measurement acceptable | **Number of patients:** 100 (55 acupuncture, 45 sham acupuncture)<br><br>**Baseline substance use:** Drug use in past 30 days: Once: 2% acupuncture, 2% sham acupuncture; Once/week: 4% acupuncture, 0% sham acupuncture; 2–3 times/week: 7% acupuncture, 9% sham acupuncture; 3–6 times/week: 7% acupuncture, 9% sham acupuncture; Once daily: 13% acupuncture, 9% sham acupuncture; 2–3 times/day: 44% acupuncture, 62% sham acupuncture; > 3 times/day: 24% acupuncture, 9% sham acupuncture<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** Acupuncture: 40.5; sham acupuncture: 40.4<br><br>**Gender:** Acupuncture: 64% male; Sham acupuncture: 73% male<br><br>**Inclusion criteria:** History of intravenous use of heroin confirmed by physical examination for signs of recent needle use<br><br>**Exclusion criteria:** Currently enrolled in a methadone detoxification program, pregnant, or on parole or probation | **Content of acupuncture intervention:** Auricular acupuncture in four ear points (kidney, lung, Shen Men, and sympathetic). Points were judged by geographic location and by client report of a tingling or a hot sensation when the targeted area was touched with a blunt instrument. No manual or electrical stimulation was employed. Acupuncture was delivered in group settings.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 20- to 45-minute sessions, 7 times a week for 3 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Methadone detoxification, entrance physical examination, counseling and discharge planning, and AIDS education<br><br>**Comparator:** Sham acupuncture (nonspecific ear points)<br><br>**Primary endpoint:** Frequency of substance use and treatment dropout at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Relapse:** Percentage of known “clean” urine samples at postintervention, versus sham acupuncture: SMD 0.05, CI −0.80 to 0.91<br><br>**Adverse events:** There was also slight bleeding at the site of needle insertion, as well as nausea, for some participants (do not know which group) |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Wells et al., 1995<br><br>**References:** Wells et al., 1995<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Test feasibility of acupuncture in methadone treatment setting<br><br>**Quality rating:** Poor<br><br>Comparable groups, reliable measurement, ITT analysis not used | **Number of patients:** 60 (31 acupuncture, 29 sham acupuncture)<br><br>**Baseline substance use:** Opiate dependence<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** 18–25: 4 participants; 26–35: 14 participants; 36–45: 32 participants; 46+: 10 participants<br><br>**Gender:** 52% male<br><br>**Inclusion criteria:** Opiates determined to be the primary drug; met federal requirements for entry into methadone treatment<br><br>**Exclusion criteria:** Pregnant; readmitted to an ongoing methadone treatment study funded by the National Institute on Drug Abuse | **Content of acupuncture intervention:** Acupuncture at five ear points (kidney, liver, lung, Shen Men, and sympathetic). Acupuncture points were located using a point-detector that measures electrical resistance. Acupuncture delivered in a group setting.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 2<br><br>**Dosage:** 40-minute sessions, 5–7 times a week for 26 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Methadone maintenance, methadone detoxification service<br><br>**Comparator:** Sham acupuncture (nonspecific ear points)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Craving during weeks when acupuncture was received, versus sham acupuncture: SMD 0.85, CI 0.32 to 1.38<br><br>**Treatment dropout:** Number of participants who completed treatment, versus sham acupuncture: OR 0.66, CI 0.22 to 2.00 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** White, Goldkamp, and Robinson, 2006<br><br>**References:** White, Goldkamp, and Robinson, 2006<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Examine the role and impact of acupuncture in the drug-court setting by studying its relationship to treatment and criminal justice outcomes<br><br>**Quality rating:** Poor<br><br>Large contamination | **Number of patients:** 336 (166 acupuncture, 170 relaxation therapy)<br><br>**Baseline substance use:** Positive drug test at entry: 48% acupuncture, 56% relaxation therapy<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** Not reported<br><br>**Gender:** Acupuncture: 79% male; relaxation therapy: 70% male<br><br>**Inclusion criteria:** Criminal drug defendants diverted to drug court<br><br>**Exclusion criteria:** Not reported | **Content of acupuncture intervention:** Auricular acupuncture by a licensed clinician<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 35- to 45-minute sessions, 5 times a week for 4.5 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Drug testing, frequent appearances in court, graduated rewards and sanctions (including selective use of jail)<br><br>**Comparator:** Active comparator (relaxation therapy)<br><br>**Primary endpoint:** Not reported<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 5 months | **Relapse:** Mean number of positive urine analyses at five-month follow-up, versus active comparator: SMD 0.00, CI −0.20 to 0.20<br><br>**Treatment dropout:** Number of participants who completed treatment, versus active comparator: OR 0.79, CI 0.49 to 1.26<br><br>**Recovery outcomes:** Number of participants with re-arrests (new charges only) at postintervention, versus active comparator: OR 0.96, CI 0.62 to 1.48 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Worner et al., 1992<br><br>**References:** Worner et al., 1992<br><br>**Country:** United States<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Evaluate the efficacy of acupuncture<br><br>**Quality rating:** Good<br><br>Proper randomization, balance at baseline, no attrition | **Number of patients:** 56 (19 acupuncture, 21 transdermal stimulation, 16 TAU)<br><br>**Baseline substance use:** One-third of the subjects reported a history of drug use in addition to alcohol. Age of first drink: 14.8 for acupuncture, 15.5 for transdermal stimulation, 17.1 for TAU; Daily drinking (in grams): 267.6 for acupuncture, 254.1 for transdermal stimulation, 239.2 for TAU<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** Acupuncture: 41.9 (SD 2.3)<br><br>**Gender:** 88% male<br><br>**Inclusion criteria:** Attending an outpatient treatment program; minimum age of 18 years; been drinking within 10 days of enrollment<br><br>**Exclusion criteria:** Resided in a halfway house; refused randomization; taking disulfiram | **Content of acupuncture intervention:** Fixed-point standardized acupuncture treatment (bilateral body points: liver 3, stomach 36, triple heater 5, large intestine 4; midline point; govenor vessel 20; bilateral ear points: Shen Men and lung). Acupuncture was performed in a group setting by a licensed acupuncturist.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30-minute sessions, 3 times a week for 13 weeks<br><br>**Type of care:** Outpatient<br><br>**Co-interventions:** Individual counseling sessions once per week, education/group therapy sessions three times per week, Alcoholics Anonymous meetings twice per week, and task-oriented group activities twice weekly<br><br>**Comparator:** (1) Active comparator (transdermal stimulation); (2) TAU (see co-interventions)<br><br>**Primary endpoint:** Treatment dropout at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** 3 months | **Relapse:** Number of subjects who either relapsed or required an inpatient detoxification at postintervention, versus active comparator: SMD −0.23, CI −0.92 to 0.46; versus TAU: SMD −0.31, CI −1.06 to 0.43<br><br>**Treatment dropout:** Number of participants who completed treatment, versus active comparator: OR 1.89, CI 0.16 to 22.75; versus TAU: OR 0.37, CI 0.01 to 9.82 |

| Study Details | Participants | Intervention/Treatment | Outcomes/Results |
|---|---|---|---|
| **Parent study:** Zeng et al., 2005<br><br>**References:** Zeng et al., 2005<br><br>**Country:** China<br><br>**Study design:** Individually randomized controlled trial<br><br>**Purpose:** Observe the effectiveness of acupuncture at points of the Du Channel in treating heroinism<br><br>**Quality rating:** Poor<br><br>Comparable groups at baseline for reported information, reliability of measurement instruments unclear, ITT analysis not used | **Number of patients:** 70 (35 acupuncture, 35 drug therapy)<br><br>**Baseline substance use:** All current heroin users<br><br>**Comorbid psychological/behavioral health conditions:** None reported<br><br>**Age (Years):** Acupuncture: 33.16 (SD 5.51); drug therapy: 34.23 (SD 4.83)<br><br>**Gender:** Acupuncture: 83.9% male; drug therapy: 80.8% male<br><br>**Inclusion criteria:** DSM-II-R diagnosis with opium drug dependence; 18–50 in age; normal finding in blood and urine routine examination; normal functions of the heart, liver, and kidney<br><br>**Exclusion criteria:** Those who had internal diseases, infectious diseases, or mental diseases; those who were unable to persist in treatment | **Content of acupuncture intervention:** A 10-day decrescendo therapy of methadone and acupuncture at points of the Du Channel were adopted in the treatment group. Acupuncture was performed at Baihui (GV 20), Dazhui (GV 14), Shendao (GV 11), Lingtai (GV 10), Zhiyang (GV 9) and Mingmen (GV 4) of the Du Channel. The needles were manipulated 3 times each session.<br><br>**Health care setting:** SUD specialty care<br><br>**Number of sites:** 1<br><br>**Dosage:** 30-minute sessions, 7 times a week for 1.5 weeks<br><br>**Type of care:** Inpatient<br><br>**Co-interventions:** Methadone therapy, given once a day at a dosage of 1 mg/kg. This dosage was daily reduced by 20% or so to 1 mg on the 10th day.<br><br>**Comparator:** Active comparator (drug therapy; see co-interventions)<br><br>**Primary endpoint:** Withdrawal/craving at postintervention<br><br>**Power calculation:** None reported<br><br>**Follow-up:** Postintervention | **Withdrawal/craving symptoms:** Withdrawal/craving symptoms on final day of treatment, versus active comparator: SMD −0.63, CI −1.16 to −0.09<br><br>**Treatment dropout:** Number of participants who completed the entire treatment process, versus active comparator: OR 0.37, CI 0.10 to 1.35 |

NOTES: “Not reported” indicates that this information was not provided in study manuscripts but was able to be reported. “None reported” indicates that this information was not provided in study manuscripts, but we do not know whether this information was relevant or collected.
SD = Standard deviation.
N/A = Not applicable.

# Appendix C: Cochrane Risk of Bias Criteria

This appendix outlines Cochrane Collaboration and U.S. Preventive Services Task Force criteria used to make risk of bias determinations.

Random sequence generation (selection bias):

- Low risk: The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random).
- High risk: The investigators describe a nonrandom component in the sequence generation process. Usually, the description would involve some systematic, nonrandom approach, for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number. Other nonrandom approaches happen much less frequently than the systematic approaches mentioned above and tend to be obvious. They usually involve judgment or some method of nonrandom categorization of participants, for example: allocation by judgment of the clinician; allocation by preference of the participant; allocation based on the results of a laboratory test or a series of tests; allocation by availability of the intervention.
- Unclear risk: Insufficient information about the sequence generation process to permit judgment of low risk or high risk.

Allocation concealment (selection bias):

- Low risk: Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomization); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.
- High risk: Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g., a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g., if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.
- Unclear risk: Insufficient information to permit judgment of low risk or high risk. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgment—for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque, and sealed.

Blinding of participants and personnel (performance bias):

- Low risk: Any one of the following: no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
- High risk: Any one of the following: no blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.
- Unclear risk: Any one of the following: insufficient information to permit judgment of low risk or high risk; the study did not address this outcome.

Blinding of outcome assessment:

- Low risk: Any one of the following: no blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
- High risk: Any one of the following: no blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.
- Unclear risk: Any one of the following: insufficient information to permit judgment of low risk or high risk; the study did not address this outcome.

Incomplete outcome data:

- Low risk: Any one of the following: no missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods.
- High risk: Any one of the following: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; as-treated analysis done with substantial departure of the intervention received from that assigned at randomization; potentially inappropriate application of simple imputation.

- Unclear risk: Any one of the following: insufficient reporting of attrition/exclusions to permit judgment of low risk or high risk (e.g., number randomized not stated, no reasons for missing data provided); the study did not address this outcome.

Selective reporting of outcome data:

- Low risk: Any of the following: the study protocol is available and all of the study's prespecified (primary and secondary) outcomes that are of interest in the review have been reported in the prespecified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified (convincing text of this nature may be uncommon).
- High risk: Any one of the following: not all of the study's prespecified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g., subscales) that were not prespecified; one or more reported primary outcomes were not prespecified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.
- Unclear risk: Insufficient information to permit judgment of low risk or high risk. It is likely that the majority of studies will fall into this category.

# Appendix D: Excluded Full-Text Articles

### *Reason Excluded: Irrelevant Outcomes*

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# Appendix E: Additional Forest and Funnel Plots

**Figure E.1. Acupuncture Versus Any Comparator on Overall Treatment Program Dropout**

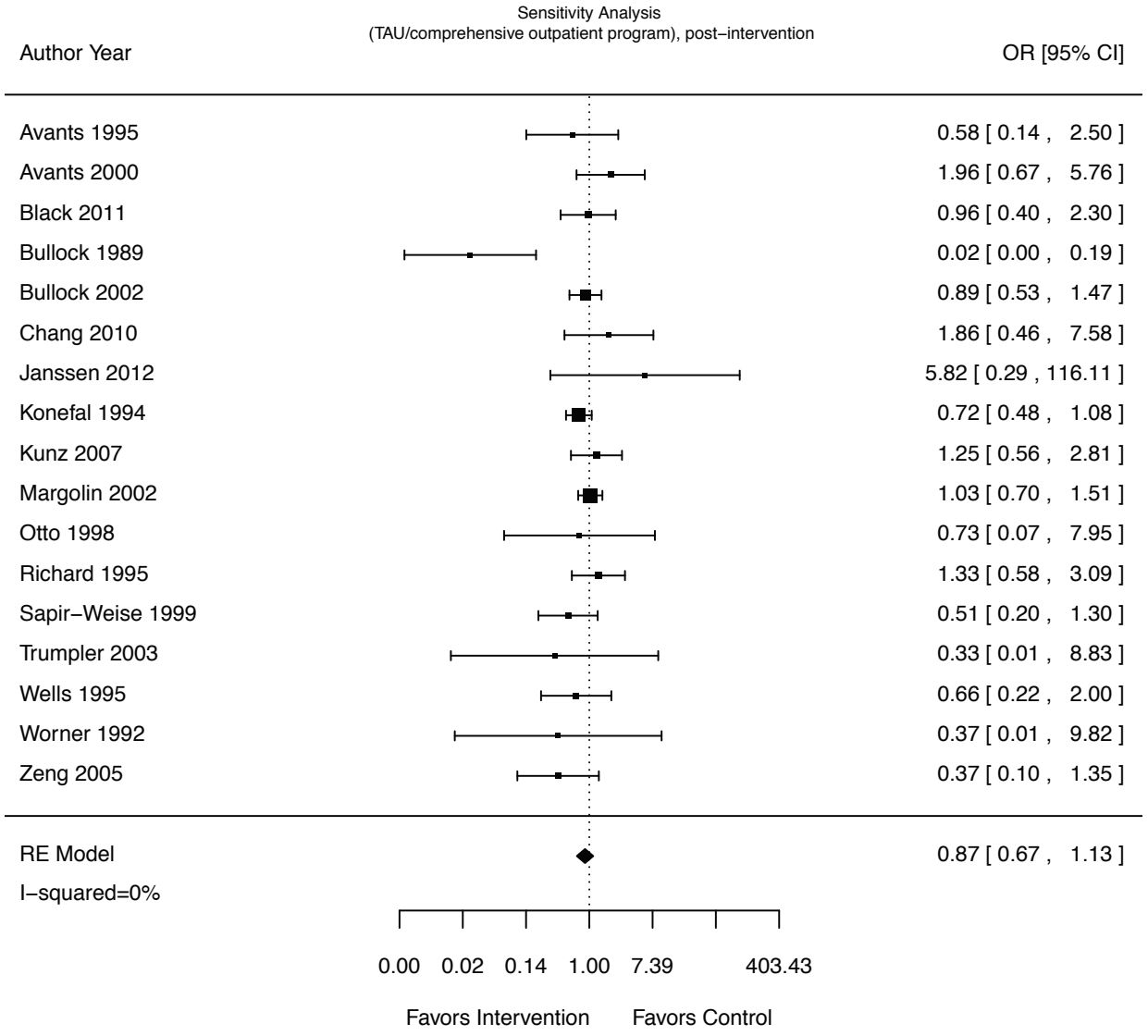
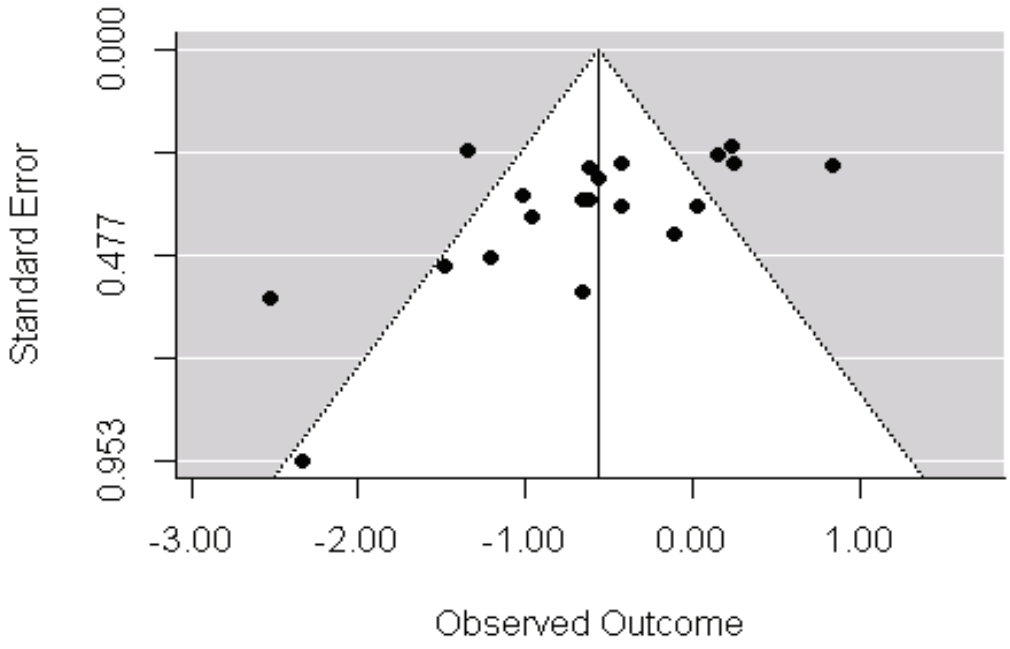


**Figure E.2. Funnel Plot for Withdrawal/Craving Symptoms**



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